ACTA · COLL · MED · PHILAD · INSTIT · A · D · MDCCLXXXVII

NON SIBI SED TOTI

TRANSACTIONS

OF THE

COLLEGE OF PHYSICIANS

OF

PHILADELPHIA

THIRD SERIES

VOLUME THE THIRTY–THIRD

NON SIBI SED TOTI
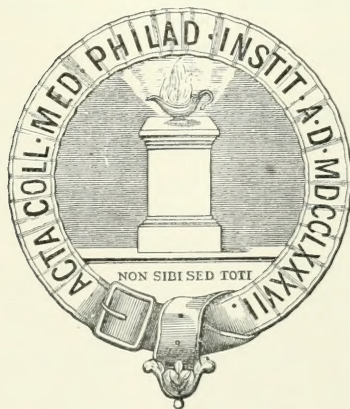
PHILADELPHIA
PRINTED FOR THE COLLEGE
1911

NOTICE

THE present volume of TRANSACTIONS contains the papers read before the College from January, 1911, to December, 1911, inclusive.

The Committee of Publication thinks it proper to say that the College holds itself in no way responsible for the statements, reasonings, or opinions set forth in the various papers published in its TRANSACTIONS.

EDITED BY

WILLIAM ZENTMAYER

COLLEGE OF PHYSICIANS OF PHILADELPHIA

1911

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[1] Died February 25, 1911.　　　　[2] Elected April 5, 1911.

LIST

PRESIDENTS OF THE COLLEGE FROM THE TIME OF ITS INSTITUTION

ELECTED

1787 JOHN REDMAN

1805 WILLIAM SHIPPEN

1809 ADAM KUHN

1818 THOMAS PARKE

1835 THOMAS C. JAMES[1]

1835 THOMAS T. HEWSON

1848 GEORGE B. WOOD

1879 W. S. W. RUSCHENBERGER

1883 ALFRED STILLE

1884 SAMUEL LEWIS[2]

1884 J. M. DaCOSTA

1886 S. WEIR MITCHELL

1889 D. HAYES AGNEW

1892 S. WEIR MITCHELL

1895 J. M. DaCOSTA

1898 JOHN ASHHURST, Jr.

1900 W. W. KEEN

1902 HORATIO C. WOOD

1904 ARTHUR V. MEIGS

1907 JAMES TYSON

1910 GEORGE E. de SCHWEINITZ

[1] Died four months after his election.
[2] Resigned on account of ill-health.

FELLOWS

COLLEGE OF PHYSICIANS OF PHILADELPHIA

DECEMBER, 1911

* Non-resident Fellows.
† Fellows who have commuted dues.

ELECTED

1892. ABBOTT, ALEXANDER C., M.D., Sc.D. (Hon.), Professor of Hygiene and Bacteriology in the University of Pennsylvania; Member of the Board of Health of Philadelphia. 4229 Baltimore Ave.

1905. ADLER, LEWIS H., JR., M.D., Professor of Diseases of the Rectum in the Philadelphia Polyclinic and College for Graduates in Medicine; formerly Prosector to the Professor of Anatomy in the University of Pennsylvania; Consulting Surgeon to the Charity Hospital; Secretary-Treasurer of the American Proctologic Society. 1610 Arch St.

1903. ALLEN, ALFRED REGINALD, M.D. Lecturer on Neurological Electro-Therapeutics and Instructor in Neurology and Neuropathology in the University of Pennsylvania. 111 S. Twenty-first St.

1906. ALLEN, FRANCIS OLCOTT, JR., A.B., M.D., Surgeon to the Dispensaries of the Presbyterian, Methodist, and Pennsylvania Hospitals. 2216 Walnut St.

1896. ALLYN, HERMAN B., M.D., Associate in Medicine in the University of Pennsylvania; Physician to the Philadelphia General Hospital. 501 S. Forty-second St.

1888. ANDERS, JAMES M., M.D., LL.D., Professor of the Theory and Practice of Medicine and Clinical Medicine in the Medico-Chirurgical College; Consulting Physician to the Jewish Hospital Association, Philadelphia. 1605 Walnut St.

ELECTED

1883. BAUM, CHARLES, A.M., M.D., PH.D.   1828 Wallace St.

1908. BEARDSLEY, EDWARD J. G., M.D., L.R.C.P. (Lond.), Chief of the Out-patient Medical Department of the Jefferson Medical College Hospital; Demonstrator of Physical Diagnosis and Clinical Medicine in the Jefferson Medical College; Physician to the Byberry Branch of the Philadelphia Hospital; Assistant Physician to the Philadelphia General Hospital.   2030 Chestnut St.

1883. BEATES, HENRY, JR., M.D., M.S., Sc.D.   260 S. Sixteenth St.

1874. BENNETT, W. H., A.M., M.D., Physician-in-Charge of the Seashore House for Invalid Children, and of the Seaside House for Invalid Women, Atlantic City; formerly Physician to the Episcopal Hospital, and Physician-in-Charge of St. Christopher's Hospital for Children.   1837 Chestnut St.

1896. BEYEA, HENRY D., M.D., Associate in Gynecology and Assistant Demonstrator of Obstetrics in the University of Pennsylvania; Assistant Surgeon to the Gynecean Hospital. 1734 Spruce St.

†1884. BIDDLE, ALEXANDER W., M.D.   Chestnut Hill.

1884. BIDDLE, THOMAS, M.D.   122 S. Twenty-second St.

*1903. BIGGS, MONTGOMERY H., M.D.   Rutherfordton, N. C.

1908. BLAND, PASCAL BROOKE, M.D., Chief Clinical Assistant in the Gynecological Department of the Jefferson Medical College Hospital; Instructor in Gynecology in the Jefferson Medical College; Gynecologist to St. Joseph's Hospital; Assistant Gynecologist to the Philadelphia General Hospital.   1729 Pine St.

1894. BLISS, ARTHUR AMES, A.M., M.D.   117 S. Twentieth St.

1894. BOCHROCH, MAX H., M.D., Demonstrator of Neurology and Chief Clinical Assistant in the Nervous Department of the Jefferson Medical College Hospital; Neurologist to the Out-patient Department of St. Joseph's Hospital.   1539 Pine St.

1896. BOGER, JOHN A., A.M., M.D., Surgeon to St. Mary's Hospital; Surgeon to the Stetson Hospital; Surgeon to the Dispensary of the Episcopal Hospital.   2213 N. Broad St.

1910. BOICE, J. MORTON, A.B., M.D., Gynecologist to the Out-patient Department of St. Joseph's Hospital; Lecturer on Chemistry to the Training School of St. Joseph's Hospital. 4020 Spruce St.

1911. BONNEY, CHARLES W., M.D., Assistant Demonstrator of Anatomy in the Jefferson Medical College; Assistant Surgeon,

Department of Oral Surgery, Philadelphia General Hospital. 1117 Spruce St.

1891. BOYD, GEORGE M., M.D., Professor of Obstetrics in the Medico-Chirurgical College; Obstetrician to the Medico-Chirurgical Hospital; Physician to the Philadelphia Lying-in Charity; Obstetrician and Gynecologist to the Philadelphia General Hospital. 1909 Spruce St.

1907. BOYER, HENRY PERCIVAL, M.D., Physician to the Stetson Hospital; Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases. 4602 Baltimore Ave.

†1884. BRADFORD, T. HEWSON, M.D., Medical Director of the Philadelphia Life Insurance Company; Medical Director of the United Security Life Insurance and Trust Company. 1802 De Lancey Place.

1907. BRADLEY, WILLIAM N., Ph.G., M.D., Physician to the Out-patient Department of the Children's Hospital; Assistant Physician to the Out-patient Department of the Pennsylvania Hospital; Assistant Physician to the Out-patient Department of the Orthopædic Hospital. 1638 S. Broad St.

1903. BRANSON, THOMAS F., M.D., Attending Physician to the Bryn Mawr Hospital. Rosemont, Pa.

1891. BRINTON, LEWIS, M.D., Physician-in-Chief of the American Hospital for Diseases of the Stomach. 1933 Spruce St.

1900. BRINTON, WARD, A.M., M.D., Visiting Physician to the Tuberculosis Department of the Philadelphia General Hospital; Visiting Physician to the Hospital for Poor Consumptives at White Haven, Pa.; Visiting Physician to the Henry Phipps Institute for the Prevention, Treatment, and Cure of Tuberculosis; Visiting Physician to the Philadelphia Jewish Sanatorium for Consumptives. 1423 Spruce St.

1907. BROOKS, MACY, A.B. (Princeton), M.D., Assistant Genito-urinary Surgeon to the Philadelphia General Hospital. 1314 Spruce St.

1887. BRUBAKER, ALBERT P., A.M., M.D., Professor of Physiology and Medical Jurisprudence in the Jefferson Medical College; Professor of Physiology and Hygiene in the Drexel Institute of Science, Art, and Industry. 105 N. Thirty-fourth St.

1851. BULLOCK, WILLIAM R., M.D. 6439 Greene St., Germantown, Phila.

ELECTED

*1897. DORLAND, W. A. NEWMAN, M.D., Professor of Obstetrics in the Medical Department of Loyola University; Visiting Gynecologist and Obstetrician to Jefferson Park Hospital; First Lieutenant, Medical Reserve Corps, U. S. Army. 1422 W. Jackson Boulevard, Chicago, Ill.

1907. DORRANCE, GEORGE MORRIS, M.D., Surgeon to St. Agnes' Hospital; Demonstrator of Applied Anatomy in the Dental Department of the University of Pennsylvania. 2025 Walnut St.

1902. DOUGHERTY, SHERBORNE W., M.D., Instructor in Physical Diagnosis in the University of Pennsylvania; Physician to the Dispensary of the German Hospital; Assistant Physician to the Methodist Hospital. 256 S. Sixteenth St.

1893. DOWNS, NORTON, M.D., Fordhooke Farms, Three Tuns, Pa.

1864. DOWNS, R. N., M.D., Consulting Physician to the Germantown Hospital. 5916 Greene St., Germantown.

1902. DOWNS, ROBERT N., JR., M.D., Surgeon to the Dispensary of the Germantown Hospital. 6008 Greene St., Germantown.

1910. DRAYTON, WILLIAM, JR., M.D., Assistant Physician to the Out-patient Department of the Pennsylvania Hospital; Clinical Assistant at the Orthopædic Hospital and Infirmary for Nervous Diseases; Physician to St. Michael's Parish School. 1316 Locust St.

1864. DUER, EDWARD L., A.M., M.D., Gynecologist to the Presbyterian Hospital; Consulting Obstetrician to the Maternity Hospital and the Preston Retreat. 1606 Locust St.

1897. DUER, S. NAUDAIN, M.D., Physician to the Dispensary of the Presbyterian Hospital. 1916 Pine St.

1871. DUHRING, L. A., M.D., Emeritus Professor of Diseases of Dermatology in the University of Pennsylvania; Honorary Member of the Dermatological Society of London, Società Itāliana di Dermatologia e Sifilographia, and Wiener Dermatologische Gesellschaft. 3322 Walnut St.

1881. DULLES, CHARLES WINSLOW, M.D., Consulting Surgeon of the Rush Hospital. 4101 Walnut St.

*1860. DUNTON, WILLIAM R., M.D., Montrose, Pa.

1911. EARNSHAW, HENRY CULP, M.D., Attending Physician to the Hospital of the Good Shepherd, Rosemont; Assistant Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Bryn Mawr Children's Hospital; Pennsylvania Railroad Surgeon. Bryn Mawr, Pa.

ELECTED

*1899. EDSALL, DAVID L., M.D., Professor of Preventive Medicine in the Washington University Medical School, St. Louis, Mo.

*1887. EDWARDS, WILLIAM A., M.D., Professor of Pediatrics in the Medical Department of the University of California. Fifth and Spring Sts., Los Angeles, Cal.

1911. ELIASON, ELDRIDGE E., B.A., M.D., Assistant Instructor in Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Assistant Surgeon to the Howard Hospital; Surgeon to the Out-patient Department of the Children's Hospital. 334 S. Sixteenth St.

1904. ELMER, WALTER G., B.S., M.D., Instructor in Orthopedic Surgery in the University of Pennsylvania; Assistant Orthopedic Surgeon to the University Hospital; Orthopedic Surgeon to the Jewish Hospital; Surgeon to the Pennsylvania Training School for Children. 1801 Pine St.

1896. ELY, THOMAS C., A.M., M.D. 2041 Green St.

1901. ERCK, THEODORE A., M.D., Associate in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Associate Surgeon to the Gynecean Hospital. 251 S. Thirteenth St.

1893. ESHNER, AUGUSTUS A., M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine; Physician to the Philadelphia General Hospital; Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Consulting Physician to Mercy Hospital. 1019 Spruce St.

*1905. EVANS, JOSEPH S., JR., A.B., M.D., Professor of Clinical Medicine and Students' Physician in the University of Wisconsin. University of Wisconsin, Madison, Wis.

1905. EVANS, WILLIAM, M.D. 4007 Chestnut St.

1894. FARIES, RANDOLPH, M.D. 2007 Walnut St.

†1903. FARR, CLIFFORD B., A.B., M.D., Professor of Diseases of the Stomach, etc., in the Philadelphia Polyclinic; Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Philadelphia General Hospital; Pathologist to the Presbyterian Hospital. 117 S. Twenty-second St.

1893. FARR, WILLIAM W., M.D., Physician to the Leamy Home. Springfield Ave. and Lincoln Drive, Chestnut Hill.

ELECTED

1903. FRANCINE, ALBERT P., A.M., M.D., Instructor in Medicine in the University of Pennsylvania; Physician to the Medical Dispensary of the University Hospital; Attending Physician to the Philadelphia General Hospital, Department of Tuberculosis; Chief Physician to the State Dispensary for Tuberculosis, Philadelphia. 218 S. Fifteenth St.

1897. FRAZIER, CHARLES H., M.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, the Philadelphia General, and the Episcopal Hospitals; Surgeon to the Home for Crippled Children. 1724 Spruce St.

†1890. FREEMAN, WALTER J., M.D., Emeritus Professor of Laryngology in the Philadelphia Polyclinic; Laryngologist to the Orthopædic Hospital; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 1832 Spruce St.

1910. FRESCOLN, LEONARD D., M.D., Chief Resident at the Episcopal Hospital, Lehigh Ave. and Front St.

1893. FRIEBIS, GEORGE, M.D., Ophthalmic Surgeon to the Lutheran Home and Orphanage, Mt. Airy. 1906 Chestnut St.

1910. FURBUSH, CHARLES LINCOLN, M.D. 1501 Spruce St.

1889. FUSSELL, M. HOWARD, M.D., Professor of Applied Therapeutics in the University of Pennsylvania; Physician to St. Timothy's Hospital; Physician to St. Mary's Hospital. 421 Lyceum Ave., Roxborough.

1899. GAMBLE, ROBERT G., M.D., one of the Attending Physicians to the Bryn Mawr Hospital. Haverford, Pa.

1873. GERHARD, GEORGE S., M.D., Physician-in-Chief to the Bryn Mawr Hospital; Consulting Physician to Bryn Mawr College; Consulting Physician to Villa Nova College. Fifty-eighth Street and Overbrook Ave.

1902. GHRISKEY, ALBERT A., M.D. 3936 Walnut St.

1892. GIBB, JOSEPH S., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic. 1907 Chestnut St.

1899. GIBBON, JOHN H., M.D., Professor of Surgery in the Jefferson Medical College; Surgeon to the Pennsylvania and the Bryn Mawr Hospitals; Consulting Surgeon to the Woman's Hospital. 1608 Spruce St.

ELECTED

1908. GILDERSLEEVE, NATHANIEL, M.D., Associate in Bacteriology in the University of Pennsylvania; Pathologist to the Bar Harbor Medical and Surgical Hospital, Bar Harbor, Me. Dormitories, University of Pennsylvania.

1897. GIRVIN, JOHN H., M.D., Physician for Diseases of Women at the Presbyterian Hospital; Instructor in Obstetrics in the University of Pennsylvania. 2120 Walnut St.

1889. GITHENS, WILLIAM H. H., M.D. 1327 Pine St.

1906. GITTINGS, J. CLAXTON, M.D., Instructor in Pediatrics in the University of Pennsylvania; Assistant Pediatric Physician to the University Hospital; Visiting Physician to the Children's Hospital, the Children's Department of the Mary J. Drexel Home, and to the Out-patient Department of the Presbyterian Hospital. 3942 Chestnut St.

1905. GIVEN, ELLIS E. W., M.D., Surgeon to the Dispensary of the Episcopal Hospital; Surgeon to the Dispensary of the St. Christopher's Hospital for Children. 2714 Columbia Ave.

1894. GLEASON, E. B., S.B., M.D., LL.D., Professor of Otology in the Medico-Chirurgical College. 2033 Chestnut St.

1906. GOEPP, R. MAX, M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Visiting Physician to the Philadelphia General Hospital; Associate in Clinical Medicine in the Jefferson Medical College. 1716 Locust St.

1906. GOLDBERG, HAROLD G., M.D., Curator and Pathologist to the Wills Eye Hospital; Assistant Ophthalmic Surgeon to the Episcopal Hospital; Secretary of the Board of Trustees, House of St. Michael and All Angels; First Lieutenant, Medical Reserve Corps, U. S. Army, N. G. P. 1905 Chestnut St.

1893. GOODELL, W. CONSTANTINE, M.D. 300 S. Thirteenth St.

1908. GOODMAN, EDWARD H., M.D., Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Medical Dispensary of the University Hospital; Dispensary Physician to the Presbyterian Hospital. 248 S. Twenty-first St.

1905. GORDON, ALFRED, M.D., Associate Member of the Société Médico-Psychologique, Paris; Neurologist to the Mt. Sinai, the Northwestern General, and the Douglass Memorial Hospitals. 1430 Pine St.

*†1897. GOULD, GEORGE M., A.M., M.D. The Sentinels, Cayuga Heights, Ithaca, N. Y.

ELECTED

1885. HARTE, RICHARD H., M.D., Adjunct Professor of Surgery in the University of Pennsylvania; Surgeon to the Pennsylvania and the Orthopædic Hospitals; Consulting Surgeon to St. Mary's, St. Timothy's, and the Bryn Mawr Hospitals. 1503 Spruce St.

1888. HARTZELL, MILTON B., M.D., LL.D., Professor of Dermatology in the University of Pennsylvania; Clinical Professor of Dermatology in the Woman's Medical College of Pennsylvania. 3644 Chestnut St.

1907. HATFIELD, CHARLES JAMES, A.B. (Princeton), M.D., Physician to the Henry Phipps Institute for the Study, Treatment, and Prevention of Tuberculosis; Visiting Physician to the White Haven Sanatorium. 2008 Walnut St.

1872. HAYS, I. MINIS, M.D. 266 S. Twenty-first St.

1882. HEARN, W. JOSEPH, M.D., Emeritus Professor of Clinical Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General Hospital. 2119 Spruce St.

1911. HEED, CHARLES R., M.D., Associate in Ophthalmology in the Philadelphia Polyclinic; Assistant Surgeon to the Wills Eye Hospital; Instructor in Ophthalmology in the Jefferson Medical College. 1700 Walnut St.

1908. HEINEBERG, ALFRED, M.D., Associate in Gynecology in the Jefferson Medical College; Assistant Gynecologist to St. Agnes' and to Mt. Sinai Hospitals. 1642 Pine St.

1901. HEISLER, JOHN C., M.D., Professor of Anatomy in the Medico-Chirurgical College. 3829 Walnut St.

1884. HENRY, FREDERICK P., A.M., M.D., Professor of the Principles and Practice of Medicine in the Woman's Medical College of Pennsylvania; Physician to the Philadelphia General Hospital; Corresponding Member of the Royal Academy of Medicine of Rome. 114 S. Eighteenth St.

1903. HENRY, J. NORMAN, M.D., Physician to the Pennsylvania Hospital; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Assistant Physician to the Philadelphia General Hospital. 1624 Spruce St.

1891. HEWSON, ADDINELL, A.M., M.D., Professor of Anatomy in the Philadelphia Polyclinic and College for Graduates in Medicine; Surgeon to St. Timothy's Hospital, Roxborough. 2120 Spruce St.

1909. HIGBEE, WILLIAM S., M.D., President of the Pennsylvania State Board of Examiners for Registration of Nurses. 1703 S. Broad St.

versity; Pathologist to the Samaritan Hospital. Temple Medical School, Eighteenth and Buttonwood Sts.

1895. McFARLAND, JOSEPH, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College; Pathologist to the Medico-Chirurgical and to the Philadelphia General Hospitals. 442 W. Stafford St., Germantown.

1905. McKENZIE, ROBERT TAIT, A.B., M.D., Professor of Physical Education and Director of the Department of Physical Education in the University of Pennsylvania. 26 S. Twenty-first St.

*1900. McREYNOLDS, ROBERT PHILLIPS, M.D. 213 S. Broadway, Los Angeles, Cal.

1886. MacCOY, ALEXANDER W., M.D., Fellow of the American Laryngological Association; Consulting Laryngologist to the Bryn Mawr Hospital. 216 S. Fifteenth St.

1901. MacLEOD, GEORGE I., JR., M.D., Physician to the Bryn Mawr Hospital; Assistant Physician to Bryn Mawr College, Ardmore, Pa.

1910. MacKINNEY, WILLIAM H., M.D., Assistant Surgeon to the Dispensary for Genito-urinary Diseases, University Hospital; Assistant in the Urological Dispensary of the German Hospital. 1701 Chestnut St.

1896. MAKUEN, G. HUDSON, M.D., Professor of Defects of Speech in the Philadelphia Polyclinic; Laryngologist to St. Mary's Hospital and to the Frederick Douglass Memorial Hospital; Visiting Consultant on Defects of Speech to the New Jersey Training School for Feeble-minded Children. 1627 Walnut St.

1898. MARSHALL, GEORGE MORLEY, M.D., Laryngologist to the Philadelphia General Hospital; Laryngologist and Otologist to St. Joseph's Hospital. 1819 Spruce St.

1893. MARSHALL, JOHN, M.D., Nat.Sc.D. (Tübingen), LL.D. Professor of Chemistry and Toxicology in the University of Pennsylvania. 1718 Pine St.

1889. MARTIN, EDWARD, M.D., John Rhea Barton Professor of Surgery in the University of Pennsylvania; Surgeon to the University, Howard, Philadelphia General, and Bryn Mawr Hospitals. 1506 Locust St.

1885. MAYS, THOMAS J., M.D., Visiting Physician to the Rush Hospital. 1829 Spruce St.

*1868. MEARS, J. EWING, A.M., M.D., LL.D. 1535 Land Title Building, Broad and Sansom Sts.

ELECTED

1905. NEWLIN, ARTHUR, B.S., M.D., Physician to the Dispensaries of the Pennsylvania Hospital and of the Children's Hospital; Assistant Physician to the Orthopædic Hospital; Associate in Pediatrics in the Philadelphia Polyclinic. 1804 Pine St.

1899. NICHOLSON, WILLIAM R., JR., M.D., Assistant Instructor in Obstetrics in the University of Pennsylvania; Obstetrician to the Maternity Hospital; Assistant Surgeon to the Gynecean Hospital. 322 S. Fifteenth St.

1889. NOBLE, CHARLES P., M.D., Surgeon-in-Charge of the Department for Women of the Northern Dispensary and of the Union Mission Hospital; Clinical Professor of Gynecology in the Woman's Medical College of Pennsylvania; Lecturer on Gynecology in the Philadelphia Polyclinic. 1509 Locust St.

1898. NOLAN, EDWARD J., M.D., Recording Secretary and Librarian of the Academy of Natural Sciences of Philadelphia. 825 N. Twentieth St.

1905. NORRIS, CHARLES C., M.D., Attending Physician to the Maternity Hospital; Instructor in Gynecology in the University of Pennsylvania; Assistant Gynecologist and Obstetrician to the Philadelphia General Hospital. 1503 Locust St.

1905. NORRIS, GEORGE WILLIAM, A.B., M.D., Assistant Professor of Medicine in the University of Pennsylvania; Physician to the Episcopal Hospital; Assistant Physician to the University Hospital; Physician to the Medical Out-patient Department of the Pennsylvania Hospital. 1530 Locust St.

*1901. NORRIS, HENRY, M.D. Rutherfordton, N. C.

*1865. NORRIS, ISAAC, M.D. Fairhill, Bryn Mawr, Pa.

1892. NORRIS, RICHARD C., M.D., Lecturer on Clinical and Operative Obstetrics in the University of Pennsylvania; Obstetrician in Charge of the Preston Retreat; Visiting Obstetrician to the Philadelphia General Hospital; Gynecologist to the Methodist Episcopal Hospital, and Consulting Obstetrician and Attending Gynecologist to the Southeastern Dispensary and Hospital. 500 N. Twentieth St.

*1884. O'NEILL, J. WILKS, M.D. Bergenfield, N. J.

*1885. OSLER, SIR WILLIAM, BART., M.D., Regius Professor of Medicine in Oxford University, England. No. 7, Norham Gardens, Oxford, England.

1903. OSTHEIMER, MAURICE, M.D., Associate in Pediatrics in the University of Pennsylvania; Physician-in-Charge of the Children's Dispensary and Assistant Visiting Pediatric Physician, University Hospital; Physician to the Medical Dispensary of the Children's Hospital; Physician to the Austro-Hungarian Consulate, Philadelphia. 118 S. Twenty-second St.

1897. PACKARD, FRANCIS R., M.D., Surgeon to the Ear, Nose, and Throat Clinic of the Pennsylvania Hospital; Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Children's Hospital of Philadelphia; Consulting Aurist to the Bryn Mawr Hospital. 304 S. Nineteenth St.

1898. PAGE, HENRY F., M.D., Assistant Physician to the German Hospital and Physician to the Medical Dispensary of the same; Instructor in Clinical Medicine in the Woman's Medical College of Pennsylvania; Physician to the Baptist Home. 1907 Girard Ave.

1906. PANCOAST, HENRY K., M.D., Professor of Röntgenology in the University of Pennsylvania and Röntgenologist to the University Hospital. 4238 Pine St.

1909. PARISH, BENJAMIN D., B.S., M.D., Assistant Instructor in Otology in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Diseases of the Ear, University Hospital; Aurist and Laryngologist to St. Agnes' Hospital. 29 S. Nineteenth St.

1899. PARKE, WILLIAM E., M.D., Consulting Obstetrician to the Episcopal Hospital; Associate Surgeon to the Kensington Hospital for Women; Gynecologist to the Frankford Hospital. 1739 N. Seventeenth St.

1910. PATTERSON, ROSS VERNET, M.D., Associate in Medicine and Sub-Dean in the Jefferson Medical College. 340 S. Sixteenth St.

1903. PEARCE, RICHARD M., M.D., Professor of Research Medicine in the University of Pennsylvania. 2114 De Lancey Place.

1909. PEMBERTON, RALPH, B.S., M.S., M.D., Woodward Fellow in Physiological Chemistry in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania; Assistant Instructor in Medicine in the University of Pennsylvania; Physician to the Out-patient Department of the Presbyterian Hospital. 2224 Locust St.

ELECTED

†1889. PENROSE, CHARLES BINGHAM, M.D., Ph.D. (Harvard), Formerly Professor of Gynecology in the University of Pennsylvania. 1720 Spruce St.

†1902. PEPPER, WILLIAM, M.D., Instructor in Medicine in the University of Pennsylvania. 1811 Spruce St.

1884. PERKINS, FRANCIS M., M.D. 332 S. Fifteenth St.

1905. PFAHLER, GEORGE E., M.D., Director of the Röntgen Ray Laboratory of the Medico-Chirurgical Hospital. 1321 Spruce St.

1907. PFROMM, GEORGE W., Ph.G., M.D. 1434 N. Fifteenth St.

1907. PHILLIPS, HORACE, M.D., Second Assistant Physician to the Pennsylvania Hospital for the Insane; Visiting Physician to the Eastern Penitentiary of Pennsylvania. Pennsylvania Hospital for the Insane.

1911. PHYSICK, EMLEN, M.D. Hotel Bellevue-Stratford.

1883. PIERSOL, GEORGE A., M.D., Professor of Anatomy in the University of Pennsylvania. 4722 Chester Ave.

1911. PIERSOL, GEORGE MORRIS, B.S., M.D., Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the University Hospital. 1927 Chestnut St.

1905. PITFIELD, ROBERT L., M.D., Pathologist to the Germantown Hospital; Bacteriologist to the Chestnut Hill Hospital for Lung Diseases. 5211 Wayne Ave.

1896. POSEY, WILLIAM CAMPBELL, M.D., Surgeon to the Wills Eye Hospital; Professor of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Howard Hospital; Ophthalmologist to the Pennsylvania Hospital for Epileptics. 2049 Chestnut St.

1899. POTTS, CHARLES S., M.D., Professor of Neurology in the Medico-Chirurgical College; Neurologist to the Philadelphia General Hospital; Consultant to the Insane Department of the Philadelphia General Hospital; Consultant to the Hospital for the Insane, Atlantic County, New Jersey. 1728 Chestnut St.

1907. PRICE, GEORGE E., M.D., Assistant Professor of Nervous and Mental Diseases in the Jefferson Medical College; Assistant Neurologist to the Philadelphia General Hospital. 1700 Walnut St.

1903. PURVES, GEORGE MOREHOUSE, M.D., Registrar of the Surgical Dispensary of the Hospital of the University of Pennsylvania. 4204 Walnut St.

sulting Ophthalmologist to the Pennsylvania Institution for the Deaf and Dumb, and to the Southern Home for Destitute Children. 109 S. Twentieth St.

1900. SHUMWAY, EDWARD ADAMS, B.S., M.D., Instructor in Ophthalmology in the University of Pennsylvania, and Assistant Ophthalmic Surgeon to the University Hospital; Assistant Ophthalmologist to the Philadelphia General Hospital; Assistant Ophthalmologist and a Chief of Clinic to the German Hospital 2007 Chestnut St.

1903. SINCLAIR, JOHN FALCONER, M.D., Physician to the Medical Dispensary of the Presbyterian Hospital; Physician to the Philadelphia Orphan Asylum and to the Presbyterian Orphanage; Physician to the Home of the Merciful Saviour for Crippled Children. 4103 Walnut St.

1907. SINKLER, FRANCIS WHARTON, A.B., M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Physician to the Episcopal Hospital. 1606 Walnut St.

1902. SITER, E. HOLLINGSWORTH, M.D., Instructor in Genitourinary Diseases in the University of Pennsylvania; Genitourinary Surgeon to the Philadelphia General Hospital; Surgeon-in-Charge of the Genito-urinary Dispensary of the University Hospital. 2038 Locust St.

1904. SKILLERN, PENN-GASKELL, M.D. 241 S. Thirteenth St.

1904. SMITH, ALLEN J., A.M., M.D., Sc.D. (Penna. Coll.), LL.D. (McGill Univ.), Professor of Pathology and of Comparative Pathology, and Director of Courses in Tropical Medicine in the University of Pennsylvania. University of Pennsylvania.

1905. SMITH, S. MACCUEN, M.D., Professor of Otology in the Jefferson Medical College; Aurist and Laryngologist to the Germantown Hospital; Aurist to the Jewish Hospital; Consulting Aurist to the Oncologic Hospital. 1429 Spruce St.

1908. SPEESE, JOHN, M.D., Instructor in Surgery in the University of Pennsylvania; Surgeon to the Dispensary of the Presbyterian, the Children's, and the Polyclinic Hospitals. 248 S. Twenty-first St.

1895. SPELLISSY, JOSEPH M., A.M., M.D., Surgeon to the Outpatient Department of the Pennsylvania Hospital; Visiting Surgeon to St. Joseph's and to the Methodist Episcopal Hospitals; Assistant Surgeon to the Orthopedic Department of the University Hospital. 110 S. Eighteenth St.

ELECTED

1898. STOUT, GEORGE C., M.D., Professor of Otology in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist and Aurist to the Presbyterian Hospital, the Children's Aid Society, and the William Penn Charter School. 1611 Walnut St.

1884. STRYKER, SAMUEL S., M.D., Physician to the Presbyterian Hospital. 3833 Walnut St.

*1900. SWAN, JOHN M., M.D. 457 Park Avenue, Rochester, N. Y.

1898. SWEET, WILLIAM M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic; Associate Professor of Ophthalmology in the Jefferson Medical College; Assistant Ophthalmic Surgeon to the Philadelphia General Hospital; Consulting Ophthalmologist to the Phœnixville Hospital. 1205 Spruce St.

1906. TAIT, THOMAS W., M.D., Ophthalmologist to the Charity Hospital. 320 S. Fifteenth St.

1900. TALLEY, JAMES ELY, A.B., M.D., Physician to the Presbyterian Hospital. 218 S. Twentieth St.

1911. TAYLOR, ALONZO ENGLEBERT, M.D., Rush Professor of Physiological Chemistry in the University of Pennsylvania. 4522 Locust St.

1886. TAYLOR, JOHN MADISON, A.B. and A.M. (Princeton), M.D., Adjunct Professor of Non-Pharmaceutical Therapeutics in the Temple University; Editor *Monthly Cyclopedia of Practical Medicine;* Consulting Physician to the Elwyn, Pa., and the Vineland, N. J., Training Schools for Feeble-minded Children. 1504 Pine St.

1887. TAYLOR, WILLIAM J., M.D., Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases; and to St. Agnes' Hospital; Consulting Surgeon to the West Philadelphia Hospital for Women. 1825 Pine St.

1886. TAYLOR, WILLIAM L., M.D. 1340 N. Twelfth St.

1910. THOMAS, BENJAMIN A., A.M., M.D., Professor of Genitourinary Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine; Instructor in Surgery in the University of Pennsylvania; Surgeon-in-Chief to the Out-patient Department of the University Hospital. 116 S. Nineteenth St.

1867. THOMAS, CHARLES HERMON, M.D. 3634 Chestnut St.

1907. THOMAS, THOMAS TURNER, M.D., Associate Professor of
Applied Anatomy, and Associate in Surgery in the Uni-
versity of Pennsylvania; Surgeon to the Philadelphia General
Hospital; Assistant Surgeon to the University Hospital.
2005 Chestnut St.

1897. THOMSON, A. G., M.D., Ophthalmic Surgeon to the Pennsyl-
vania Railroad Company.   1516 Locust St.

1896. THORINGTON, JAMES, A.M., M.D., Professor of Diseases of
the Eye in the Philadelphia Polyclinic and College for
Graduates in Medicine; Ophthalmic Surgeon to the Presby-
terian Hospital; Consulting Ophthalmologist to the American
Hospital for Diseases of the Stomach; Ophthalmologist
to the Ellwyn, Pa., and the Vineland, N. J., Training Schools
for Feeble-minded Children.   2031 Chestnut St.

1898. THORNTON, EDWARD Q., M.D., Assistant Professor of Materia
Medica in the Jefferson Medical College.   1331 Pine St.

1896. TOULMIN, HARRY, M.D., Medical Director of the Penn
Mutual Life Insurance Company.   925 Chestnut St.

1908. TRACY, STEPHEN E., M.D., Gynecologist to the Stetson
Hospital.   1527 Spruce St.

1901. TUCKER, HENRY, M.D.   2000 Pine St.

†1894. TUNIS, JOSEPH PRICE, M.D., Clinical Assistant to the Nose
and Throat Dispensary of the Polyclinic Hospital.   St.
Martin's, Philadelphia.

1901. TURNER, JOHN B., M.D.   1833 Chestnut St.

1866. TYSON, JAMES, M.D., LL.D., Emeritus Professor of Medicine
in the University of Pennsylvania and late Physician to
the Hospital of the University of Pennsylvania; Physician
to the Pennsylvania Hospital.   1506 Spruce St.

1897. TYSON, T. MELLOR, M.D., Physician to the Philadelphia
General Hospital; Assistant Physician to the Hospital of
the University of Pennsylvania; Physician to the Rush
Hospital, the Philadelphia Lying-in-Charity Hospital, and
the Children's Aid Society of Philadelphia.   1506 Spruce St.

1904. UHLE, ALEXANDER A., M.D., Assistant Instructor in Genito-
urinary Diseases in the University of Pennsylvania; Assist-
ant Surgeon to the Dispensary for Genito-urinary Diseases,
University Hospital; Assistant Genito-urinary Surgeon to
the Philadelphia General Hospital; Assistant Surgeon
to the Dispensary of the German Hospital.   1327 Jeffer-
son St.

1907. ULLOM, JOSEPHUS TUCKER, A.B., M.D., Member of the Staff of the Henry Phipps Institute for Tuberculosis. 24 Carpenter St., Germantown.

1873. VAN HARLINGEN, ARTHUR, Ph.B. (Yale), M.D., Emeritus Professor of Diseases of the Skin in the Philadelphia Poly-clinic; Dermatologist to the Children's Hospital. 1831 Chestnut St.

1903. VAN PELT, WILLIAM TURNER, M.D., Ophthalmic Surgeon to the Episcopal Hospital. 1528 Spruce St.

1893. VANSANT, EUGENE LARUE, M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Visiting Physician to the Throat, Nose, and Ear Department of the Howard Hospital. 1929 Chestnut St.

*1897. VEASEY, CLARENCE A., A.M., M.D., Formerly Assistant Professor of Ophthalmology in the Jefferson Medical College, and Assistant Ophthalmologist to the Jefferson Medical College Hospital; Formerly Ophthalmic Surgeon to the Methodist Episcopal Hospital, Philadelphia. Suite 205, Traders' Bank Building, Spokane, Wash.

†1883. VINTON, CHARLES HARROD, A.M., M.D. Hotel New Chatham, Atlantic City, N. J.

1903. WADSWORTH, WILLIAM SCOTT, M.D. 207 S. Forty-fifth St.

1906. WALKER, JOHN K., M.D., Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Dispensary of the Mary J. Drexel Home. 1632 Spruce St.

1907. WALKER, WARREN, M.D., Surgeon to the Dispensary of the Episcopal Hospital; Surgeon to the Dispensary of the Children's Hospital; Assistant Surgeon in the Clinic for Genito-urinary Diseases of the Polyclinic Hospital. 1632 Spruce St.

1904. WALSH, JOSEPH, A.M., M.D., Visiting Physician to the White Haven Sanatorium and Vice-President of the Board of Directors; Consulting Physician to the Department of Tuberculosis at the Philadelphia General Hospital; Medical Director of St. Agnes' Hospital. 732 Pine St.

1910. WARD, E. TILLSON, A.M., M.D. 1415 S. Broad St.

1893. WARREN, JOSEPH W., M.D., Associate Professor of Physi-ology in Bryn Mawr College. Bryn Mawr, Pa.

ELECTED

1895. Watson, Arthur W., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Jewish Hospital; Laryngologist and Aurist to the Mt. Sinai Hospital; Laryngologist to the Home for Incurables. 126 S. Eighteenth St.

1886. Watson, Edward W., M.D., Physician to the Magdalene Home.   38 S. Nineteenth St.

1903. Weber, Charles H., M.D., Physician to the Dispensary of the Children's Hospital.   2048 Pine St.

1906. Weisenburg, Theodore H., M.D., Professor of Clinical Neurology and of Neuropathology in the Medico-Chirurgical College; Neurologist to the Philadelphia General Hospital; Consulting Neurologist to the State Hospital for the Insane at Norristown and to the State Hospital for the Feeble-minded and Epileptic at Spring City.   2030 Chestnut St.

1883. Welch, William M., M.D., Chief Diagnostician to the Bureau of Health, and Consulting Physician to the Municipal Hospital for Contagious Diseases; Consulting Physician to the Northern Dispensary and the Northern Home for Friendless Children.   1411 Jefferson St.

1897. Wells, William H., M.D., Associate in Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson Medical College Hospital.   1135 Spruce St.

1893. Westcott, Thompson S., M.D., Associate in Diseases of Children in the University of Pennsylvania; Visiting Physician to the Methodist Episcopal Hospital; Assistant Physician to the Children's Hospital; Pediatrist to the Jewish Hospital.   1720 Pine St.

1884. Wharton, Henry R., M.D., Surgeon to the Presbyterian and the Children's Hospitals; Surgeon to Girard College; Consulting Surgeon to the Bryn Mawr Hospital, the Chestnut Hill Hospital, St. Christopher's Hospital for Children, the Pennsylvania Institution for the Deaf and Dumb, and the Pennsylvania Institution for the Blind.   1725 Spruce St.

1901. White, Courtland Y., M.D., Director of the Pathological Laboratories of the Episcopal Hospital; Pathologist to the Children's Hospital and to the Kensington Hospital for Women; Chief Bacteriologist to the Bureau of Health, Department of Health and Charities, Philadelphia.   1808 Diamond St.

ELECTED

1878. WHITE, J. WILLIAM, M.D., Ph.D., LL.D. (Hon., Aberdeen), Fellow of the American Surgical Association and of the American Association of Genito-urinary Surgeons. 1810 S. Rittenhouse Square.

1905. WHITEWAY, HAROLD M., M.D. 1924 Chestnut St.

1898. WHITING, ALBERT D., M.D., Surgeon to the Germantown Hospital; Assistant Surgeon to the German Hospital; Surgeon to the Southern Home for Destitute Children; Surgeon to the Out-patient Department of the German Hospital; Instructor in Surgery in the University of Pennsylvania. 1523 Spruce St.

1907. WILLIAMS, CARL, B.S., M.D., Assistant Ophthalmic Surgeon to the Germantown Hospital; Assistant Surgeon to the Dispensary for Diseases of the Eye at the University Hospital. N. E. cor. Schoolhouse Lane and Greene St., Germantown.

1902. WILLSON, ROBERT N., JR., M.D., Pathologist to the Presbyterian Hospital; Assistant Physician to the Philadelphia General Hospital. 1708 Locust St.

1881. WILSON, H. AUGUSTUS, M.D., Professor of Orthopedic Surgery in the Jefferson Medical College; Emeritus Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Consulting Orthopedic Surgeon to the Philadelphia Lying-in Charity Hospital and the Kensington Hospital for Women; Senior Orthopedic Surgeon to the Philadelphia General Hospital. 1611 Spruce St.

1874. WILSON, JAMES C., A.M. (Princeton), M.D., Emeritus Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College; Physician-in-Chief to the German Hospital; Attending Physician to the Pennsylvania Hospital; Consulting Physician to the Bryn Mawr Hospital. 1509 Walnut St.

1902. WILSON, SAMUEL M., M.D. 1517 Arch St.

1897. WILSON, W. REYNOLDS, M.D., Visiting Physician to the Philadelphia Lying-in-Charity Hospital. 1709 Spruce St.

1904. WISTER, JAMES W., M.D., Physician to the Out-patient Department of the Germantown Hospital. 5430 Germantown Ave.

*1901. WITMER, A. FERREE, M.D., Freeport, Long Island, N. Y.

1893. WOOD, ALFRED C., M.D., Assistant Professor of Surgery in the University of Pennsylvania; Surgeon to the University, the Philadelphia General, St. Timothy's, and the Howard Hospitals. 128 S. Seventeenth St.

1899. ZIEGLER, S. LEWIS, A.M., M.D., Sc.D., Attending Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to St. Joseph's Hospital; Membre Société Française d'Ophtalmologie. 1625 Walnut St.

1887. ZIEGLER, WALTER M. L., A.M., M.D. 1418 N. Seventeenth St.

1895. ZIMMERMAN, MASON W., M.D., Consulting Ophthalmic Surgeon to the Germantown Hospital. 1522 Locust St.

ASSOCIATE FELLOWS

AMERICAN

ELECTED

1911. ABBE, ROBERT, M.D. 13 W. Fiftieth St., New York City, N. Y.

1909. BILLINGS, FRANK, M.D., 335 E. Twenty-second Street, Chicago, Illinois.

1876. BILLINGS, JOHN S., M.D., U. S. A., Astor Library Building, 40 Lafayette Place, New York City, New York.

1877. CHAILLE, STANFORD E., M.D., University Building, New Orleans, Louisiana.

1886. CHEEVER, DAVID W., M.D., 557 Boylston Street, Boston, Massachusetts.

1893. COUNCILMAN, WILLIAM T., M.D., Harvard Medical College, Boston, Massachusetts.

1909. CRILE, GEORGE W., M.D., 1021 Prospect Avenue, S. E., Cleveland, Ohio.

1909. DANA, CHARLES LOOMIS, M.D., 53 West Fifty-third Street, New York City, New York.

1892. EMMET, THOMAS ADDIS, M.D., 91 Madison Avenue, New York City, New York.

1892. FITZ, REGINALD H., M.D., 81 Arlington Street, Boston, Massachusetts.

1895. FLETCHER, ROBERT, M.D., Army Medical Museum, Washington, D. C.

1903. GORGAS, WILLIAM C., M.D., U. S. A., Washington, D. C.

1891. JACOBI, A., M.D., 19 East Forty-seventh Street, New York City, New York.

1895. McBURNEY, CHARLES, M.D., 28 West Thirty-seventh Street, New York City, New York.

1909. MALL, FRANKLIN P., M.D., 1514 Bolton Street, Baltimore, Maryland.

1906. MAYO, WILLIAM J., M.D., Rochester, Minnesota.
1906. PILCHER, LEWIS STEPHEN, M.D., 386 Grand Avenue, Brooklyn, New York.
1886. REEVE, JOHN C., M.D., LL.D., S. W. corner Third and Wilkinson Streets, Dayton, Ohio.
1906. SHATTUCK, FREDERICK C., M.D., 135 Marlborough Street, Boston, Massachusetts.
1896. STERNBERG, GEORGE M., M.D., U. S. A., 1019 Sixteenth Street, N. W., Washington, D. C.
1896. TIFFANY, L. McLANE, M.D., 831 Park Avenue, Baltimore, Maryland.
1909. WADSWORTH, OLIVER F., M.D., 526 Beacon Street, Boston, Massachusetts.
1894. WARREN, J. COLLINS, M.D., 58 Beacon Street, Boston, Massachusetts.
1894. WEIR, ROBERT F., M.D., 11 East Fifty-fourth Street, New York City, New York.
1892. WELCH, WILLIAM H., M.D., Johns Hopkins Hospital, Baltimore, Maryland.

FOREIGN

1890. BACCELLI, GUIDO, Rome, Italy.
1908. BANNERMAN, W. B., M.D., Lt. Col. I. M. S., 11 Strathearn Place, Edinburgh, Scotland.
1894. BRUNTON, SIR T. LAUDER, M.D., 10 Stratford Place, London, W., England.
1903. FINLAY, CHARLES J., M.D., Havana, Cuba.
1899. FRASER, SIR THOMAS R., M.D., LL.D., F.R.C.P., F.R.S., 13 Drumsheigh-Gardens, Edinburgh, Scotland.
1903. HORSLEY, SIR VICTOR ALEXANDER HADEN, F.R.S., 25 Cavendish Square, London, England.
1906. HUTCHINSON, JONATHAN, M.D., LL.D., F.R.S., 15 Cavendish Square, London, W., England.
1896. JACCOUD, PROF. S., Rue Tronchet 35, Paris, France.
1894. JACKSON, J. HUGHLINGS, M.D., 3 Manchester Square, London, England.
1893. VON JAKSCH, RUDOLF, M.D., Prague, Bohemia.
1903. KOCHER, PROF. THEODOR, M.D., Berne, Switzerland.
1877. LORD LISTER, M.D., LL.D., F.R.S., 12 Park Crescent, Portland Place, London, W., England.

CORRESPONDING MEMBERS

1880. CARROW, FLEMMING, M.D., Washington Arcade, Detroit, Michigan.

1880. CHIARA, DOMENICO, M.D., Florence, Italy.

1886. DEY, KANNY LALL, M.D., Calcutta, India.

1885. RENDU, JEAN, M.D., Lyons, France.

NECROLOGICAL LIST

FELLOWS

ALOYSIUS O. J. KELLY,   February 25, 1911
CHARLES A. OLIVER,   April 8, 1911
JOHN B. SHOBER,   April 27, 1911
MICHAEL T. PRENDERGAST,   June 3, 1911
JOSEPH PRICE,   June 6, 1911
EDWARD SHIPPEN,   June 16, 1911

ASSOCIATE FELLOWS

ERNST LEYDEN,   October 5, 1910
EDWARD G. JANEWAY,   February 10, 1911
HENRY P. BOWDITCH,   March 13, 1911

CONTENTS

APPENDIX

MEMOIR OF JOHN DUTTON STEELE, M.D.[1]

By JOHN H. MUSSER, M.D.

THE fine tribute paid to that function of the College the fellowship of books and the fellowship of men, by which younger members of the profession with high ideals and aspirations are stimulated, and for which they seek early membership, is often filled with pathos. Too often their hopes are not realized from failing health or early death. From memory alone the writer can glean the following illustrations: At the time of my entrance into the medical profession the sorrow of the Fellows of the College for the loss of three brilliant members of the organization, Edward Rhoads, George Pepper, and Louis Stille, was not assuaged. Shortly after this period, grief was rekindled by the death of two of my teachers, John S. Parry and Robert Binney Hare. None knew them but to love them, none named them but to praise.

Passing over, for the writer a rather too long period of time during which sorrow was repeatedly rehabilitated, we come to later years when again the College is in tears at the untimely death of two of its most beloved members, Fred. Packard and J. Alison Scott. To this list of noble souls we can fittingly place the subject of this memoir.

It was the fetish for each one of these men to uphold the noble traditions and ideals of their chosen profession and to pursue truth for truth's sake, let its pathway lead whither it may. The earlier of these Fellows—my teachers, and the latter—my pupils, assistants, and associates in teaching and practice, it is but a small tribute to their worth for the writer to speak of the stimulus derived by him from this association.

[1] Read April 5, 1911.

John Dutton Steele was born in Sterling, New York, on February 21, 1868. His family was one of that strong colony of early settlers whose energy and enterprise and probity made the Schuylkill Valley famous in the early industries of Pennsylvania. His early education was obtained at the Hill School in Pottstown, the town which his family adopted. He graduated from Williams College in 1888 and in 1893 from the medical department of the University of Pennsylvania. He led his class in this institution and was awarded the alumni medal. He served as interne at the Philadelphia Hospital and studied in Germany and Austria. He was made assistant demonstrator of anatomy, then instructor in medicine, and finally Associate in Medicine in the University of Pennsylvania. He was clinical pathologist and later visiting physician to the Presbyterian Hospital.

He was a member of the Philadelphia County Medical Society; of the Medical Society of the State of Pennsylvania; of the American Medical Association; of the Philadelphia Pathological Society. He was made an Associate Member of the Association of American Physicians in 1905, and finally, on May 13, 1908, he was elected a full member of the Association. He was at this time a very ill man. He was not too ill, however, to appreciate this recognition of his splendid work.

Dr. Steele's best work was on lines of clinical research. His papers on Gastric Hyperesthesia, on Gastroptosis, on Dilatation of the Stomach and on Chronic Constipation were illuminating, and his studies of the feces brought many interesting features to the light. His best clinical papers were on Retroperitoneal Sarcoma and on Pleural Effusion in Heart Disease. His last publication was prepared during his final illness, which terminated fatally at Wayne, Pennsylvania, on May 17, 1908.

Thus passed away a character the mortal encasement of which was too frail to hold for long. Yet who that knew him can forget the genial smile, the well of sympathy, the fire of intellect, that lent to his delicate countenance a charm that portrayed the idealism of the spirit. When he sought truth it was as the war horse scenting the battle afar with relentless energy, uncom-

promising toil; when he found it, it was as if a priceless treasure had been placed in his hands.   When he filled the role of teacher he secured the sympathy of his students, aroused their greed for knowledge, and stimulated their ideals.   When he practised medicine, untiring devotion, kindly sympathy, clear intellect, and vision, invoking a hallowed confidence from his patients, attended his footsteps.

A large number of lay and professional friends attended the last rites of affection and respect, and followed to the grave the mortal remains of one of our most congenial and sympathetic Fellows.

MEMOIR OF GEORGE CUVIER HARLAN, M.D.[1]

By JOHN B. SHOBER, M.D.

On Wednesday afternoon, September 23, 1909, while riding along the banks of the Wissahickon near Chestnut Hill, Dr. George C. Harlan fell with his horse over an embankment, and sustained injuries of such a serious nature that he died early the following Saturday morning.

On the day of the accident, when the news was published in the papers, many of his friends, composed largely of the leading members of the medical profession and Fellows of the College of Physicians, made a pilgrimage to the Chestnut Hill Hospital; and the few who had the melancholy satisfaction of seeing him will long remember the patient resignation and courageous fortitude with which he approached his grave—

> "Sustained and soothed by an unfaltering trust, . . .
> Like one who wraps the drapery of his couch
> About him, and lies down to pleasant dreams."

George Cuvier Harlan was born in Philadelphia, Pennsylvania, on January 28, 1835, and died September 25, 1909, in the seventy-fifth year of his age. He was the son of the distinguished physician and naturalist Dr. Richard Harlan, who was born in Philadelphia, September 19, 1796, and died at New Orleans, Louisiana, September 30, 1843, and who previous to his graduation from the Medical Department of the University of Pennsylvania in 1818 made a voyage to Calcutta as surgeon of an East Indian ship, and before his return visited many of the European medical centres

of learning and formed friendships that were of life-long duration.
He practised his profession in Philadelphia, and in 1821 he was
elected Professor of Comparative Anatomy in the Philadelphia
Museum. During the cholera epidemic of 1832 the City Councils
sent a commission of medical advisers, consisting of Dr. Samuel
Jackson, Dr. Charles D. Meigs, and Dr. Richard Harlan, to visit
Canada and New York, where the ravages of the disease were
greater than they became here; and upon their return, he with
other members of the Sanitary Commission, among whom were
Dr. Nathaniel Chapman and Dr. Joseph Parrish, took charge of
temporary hospitals and held the disease in check. In recognition
of these services, Councils awarded to the members of the Commis-
sion handsome memorials. Dr. Harlan received a massive silver
pitcher, which bears this inscription:

<div align="center">

TO
DR. RICHARD HARLAN
THE CITY OF PHILADELPHIA
GRATEFUL FOR HIS DISINTERESTED AND
INTREPID SERVICES IN A PERIOD OF
PUBLIC CALAMITY
TRANSIAT IN EXEMPLUM
CHOLERA EPIDEMIC, 1832

</div>

Dr. Richard Harlan was best known to the public as the author
of works on natural history. In 1825 he published his *Fauna
Americana, or Catalogue of American Mammiferous Animals*.
In 1835 he collected most of his essays which had previously
appeared on medical subjects and on geology, zoölogy, and com-
parative anatomy, and published them, with various additions,
in a volume entitled *Medical and Physical Researches*, which,
with his former volume, attracted the notice of the most eminent
European naturalists. In 1839, he visited Europe for the second
time, and was treated with marked distinction. He was one of
the founders of the Société Cuivierienne of Paris, and was a member
of many scientific societies here and abroad, among which may be
mentioned: The Royal Museum of Natural History, of Paris; the
Royal Academy of Medicine, of Sweden; the Wernerian Natural

History Society, of Edinburgh; the Geological Society, of France; and the Boston Natural History Society. He was an honorary member of the Asiatic Society, of Bengal, and also of the Medical Society of Kent, England, and was a member of the New York Lyceum of Natural History, the American Philosophical Society, the Academy of Natural Sciences of Philadelphia, etc. He occupied the position of surgeon to the Philadelphia General Hospital. He enjoyed a life-long friendship with the French naturalist Cuvier, with whom he was in constant correspondence until his death, and after whom he named his son, the subject of this memoir.

After his return from abroad, near the close of the year 1842, Dr. Richard Harlan removed to New Orleans, where he purposed to establish himself, and where he at once took a leading position in the profession, and was elected vice-president of the Louisiana State Medical Society; but on September 30, 1843, he died suddenly of apoplexy, at the age of forty-seven, leaving a widow and four children, of whom George Cuvier was the eldest, being then eight years of age. The family, left in moderate circumstances, immediately settled in Burlington, New Jersey, the home of Mrs. Harlan's relatives. Later they moved to Wilmington, Delaware, where they remained until about 1856.

Inspired by the example of his distinguished father, George Cuvier Harlan, at an early age, determined to devote his life to the medical profession. Accordingly, at the age of sixteen, he was matriculated in Delaware College, receiving the degree of B.A. in 1855 and the Master's degree three years later. In 1858 he was graduated from the Medical Department of the University of Pennsylvania, his inaugural thesis being upon the subject of "The Iris," thus showing how early in his career he became interested in the specialty to which he subsequently devoted all his energies, and in which he became so eminent. As a further indication of his early interest in ophthalmology, he accepted an appointment as resident physician in the Wills Hospital of Philadelphia in 1857, this being his last year in the medical school. The faithfulness with which he performed his duties in this his

first medical appointment, and the charming qualities of mind
and temperament that throughout his long and honorable life
impressed themselves upon all with whom he came in contact,
are attested by a memorial signed by the visiting surgeons of the
Hospital, and sent to him at the expiration of his term of service:

Dr. George C. Harlan, late Resident Physician of the Wills Hospital
for Diseases of the Eye and Limb, having completed the term of service
for which he was elected, the undersigned Surgeons to that Institution
have great pleasure in expressing their high sense of the fidelity and
ability with which he has performed the duties of that office. It has
been held by many able and excellent individuals, some of whom now
occupy distinguished positions in the profession, but by none more
worthily than by him, whether we regard his uniform courtesy to all,
his kindness and attention to the patients, his zeal in the acquisition of
knowledge, or the tact and skill which he has displayed in practice.
The close relationship which we have had with him has afforded us
ample opportunities for forming a correct judgment in these particulars,
and now that it has been severed by the expiration of his official term,
we part from him with regret, and heartily recommend him as one whose
amiable disposition and honorable conduct must secure universal respect
and esteem, and whose professional attainments abundantly qualify
him to fill with credit to himself and advantage to others any position
to which he may aspire.

<div align="center">
S. Little, M.D.,
Wm. Hunt, M.D.,
Edward Hartshorne, M.D.,
Addinell Hewson, M.D.,
<i>Attending Surgeons of Wills Hospital for
Diseases of the Eye and Limb.</i>
</div>

Philadelphia, April, 1858.

The promise of a useful and honorable career foreshadowed in
this spontaneous and unusual expression of regard was not to be
disappointed. Immediately after receiving his medical degree,
in 1858, he served a term as resident physician in St. Joseph's
Hospital; and on March 3, 1859, he was elected resident physician
to the Pennsylvania Hospital, which institution and the Wills
Eye Hospital became in later years the scenes of his greatest
activities and brought to him a reputation which has placed his
name high in the annals of American ophthalmology.

At the beginning of the War of the Rebellion, on May 21, 1861, he was appointed Acting Assistant Surgeon in the United States Navy, and was assigned to the gunboat "Union," on blockading duty off the coast of Virginia. Desiring, however, a more active service, he soon succeeded in being transferred from the navy, and on the 14th of the following September he was appointed Major and Surgeon in Harlan's Light Cavalry, under his uncle Colonel Josiah Harlan, who had organized it as an independent regiment during the months of August and September, 1861, under special authority from the Secretary of War. It having been ascertained a few months later that Congress had only authorized the raising of regiments by States, and that consequently the formation of Harlan's Light Cavalry as an independent regiment was irregular, it was attached to the Pennsylvania State organization on November 13, 1861, and received the official designation of "The Eleventh Regiment of Pennsylvania Cavalry Volunteers."

Throughout the war the regiment was engaged in picket, scouting, and patrol duty in the neighborhood of Fortress Monroe, and saw much active service on many raids into the enemy's territory. Dr. Harlan was ever solicitous for the welfare of his men, and his camps were models of cleanliness and sanitation. As a result, there was very little sickness, due to preventable diseases among the troops under his care. His reputation in this regard won for him, in June, 1863, the appointment of Acting Medical Inspector for the Division.

His bi-weekly letters to his mother, extending over a period of three years, are full of enthusiasm and interest in his work, and reflect a fine sense of humor, which, with a natural charm of manner and nobility of character that impressed itself on all, made him one of the most popular officers of the regiment. In one of his letters, referring to a bill for the repair of instruments, he writes: " I will have it charged to Uncle Sam under the head of 'Butter and eggs, milk, chickens,' or something of that kind; as the red-tape arrangements have made no allowance for the repair of instruments, and literal honesty would cost me six dollars. As you will probably suspect, expediency enters more extensively into my code of

morals than it used to do in the old times of peace and innocence, and sometimes just a little stretching of the conscience enables me to obtain things for the hospital that we would otherwise have to do without. My new hospital has even been roofed with omelets, chicken soup, etc. In these rough times we can get along a good deal better without a conscience than without a roof."

From June 21 to 30, 1864, the regiment was engaged with Kautz's and Wilson's divisions, having for its object the destruction of the Danville Railroad. The command, nearly ten thousand strong, moved out from the rear of Petersburg and conducted a most successful raid. In returning, a strong force of the enemy's cavalry was encountered at Stony Creek, on the night of the 28th, and at Ream's Station, on the 29th, heavy engagements took place, in which both divisions suffered severely. In the charge of the Eleventh, on the last day, many brave and gallant officers and men fell. Dr. Harlan, who voluntarily remained on the field attending the wounded, was captured and sent to Petersburg, and afterward to Libby Prison, where he was detained, and where he did much to mitigate and relieve the sufferings of the sick and injured, sharing their hardships and privations, until he was released early in September. His term of service having expired, he resigned his commission and was honorably discharged September 28, 1864. Declining a very flattering offer of an appointment as surgeon on the staff of General Kautz, Division Commander, and amid sincere expressions of regret on the part of Colonel Francis A. Stratton and the officers and men of his regiment, he returned to Philadelphia and entered at once upon the practice of his profession.

While he was in the army, from 1861 to 1864, he held the position of attending surgeon to the Wills Eye Hospital. He resigned in 1864, and four years later, in 1868, he was reëlected, and continued in active service until shortly before his death.

On October 17, 1866, Dr. Harlan married Mary D. Holman, daughter of S. Atherton and Lucy Cushing Holman, of Boston. He had already succeeded in building up a lucrative practice in the line of his specialty, and was recognized as one of the leading

ophthalmologists of Philadelphia.   Dr. Charles A. Oliver, who
for many years was associated with Dr. Harlan in much of his
hospital work, has written the following summary of his career:[1]

"In 1875 he became ophthalmologist (afterward consulting
ophthalmologist) to the Pennsylvania Institution for the Instruc-
tion of the Blind, at which place he made many scientific investi-
gations and did much clinical work.   His interest in the welfare
of the eyes of the children there placed under his charge never
lessened.

"Four years later he became connected with the Eye and Ear
Department of the Pennsylvania Hospital, which he raised to the
high standard of efficiency that it at present maintains.   He served
in the same capacity in the Children's Hospital.   At the time
of his death, he occupied the position of emeritus surgeon at the
former institution.

"His ophthalmic work, so cheerfully done at the Pennsylvania
Institution for the Deaf and Dumb as consulting ophthalmologist
was commenced in 1883 and continued until the time of his death.

"He had the honor of occupying the first chair of ophthal-
mology (later emeritus) at the Philadelphia Polyclinic and School
for Graduates in Medicine.   His remarkable teaching abilities will
be long remembered by many of his students.   His exposition of
the subject was properly limited to practicalities, no attempt
for self-laudation or exhibition of rapid and useless—and, as we
have too often seen, destructive—operative procedure ever being
made.

"Among his most important memberships in societies may be
mentioned: The College of Physicians of Philadelphia in 1865,
the American Ophthalmological Society in 1873, the Wills Hos-
pital Ophthalmic Society from its foundation, the International
Congress of Ophthalmology in 1876, the Philadelphia County
Medical Society in 1876, the Medical Society of the State of
Pennsylvania, the American Medical Association, and the Ameri-
can Otological Society in 1882.

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[1] Transactions of the American Ophthalmological Society, vol. xii, Part II.

"He was a member of the University Club of Philadelphia, and a Companion of the First Class of the Military Order of the Loyal Legion of the United States.

"He enjoyed many honors. In 1885 he was made a member of the Committee on Library of the College of Physicians of Philadelphia, acting as Chairman of the Committee for many years (from 1894 until his death). In 1893 he was elected president of the American Ophthalmological Society, and in 1904 he was appointed Chairman of the Section on Ophthalmology at the Universal (Louisiana Purchase) Exposition held in St. Louis, Missouri. . . .

"His contributions to his special branch of medicine have been important and numerous. For a long period of time his little book, entitled *Eyesight and How to Care for It*, published in 1879, enjoyed a large and useful circulation. His two articles on 'Diseases of the Eyelids' and 'Operations Performed upon the Eyelids,' in the third volume of Norris and Oliver's *System of Diseases of the Eye*, must be ranked among the highest and the most practical expositions of the subject that we have in ophthalmology. At the time of his death he was associated with the editorial staff of the widely known journal *Ophthalmology*. His operation for symblepharon and his tests for malingering are broadly known and are extensively employed. . . . As an operator he stands *par excellence* as one of the most careful, the most conscientious, and the most successful of all special surgeons. . . . He was ever eminent for all manner of important hints, judicious helps, and best methods of procedure. Always calm amid danger, sure as to action, and ofttimes turning an apparently disastrous result into an advantageous one, he was *facile princeps*. The cunning of his hands was constantly in absolute correlation with deliberate, and yet rapid, judgment. Many a time when, through some misadventure, an apparently smooth piece of operative work has necessitated an impromptu difference of action, has he quickly discussed the modification and made the change in such a manner as to give the utmost good of result. It was a pleasure for any conscientious and progressive man to be near and with him under such circumstances."

The following extracts from a letter written by Dr. Francis R. Packard, on March 23, 1910, to Dr. John B. Shober give an account of Dr. Harlan's connection with the Pennsylvania Hospital:

"On October 27, 1879, Dr. Harlan was elected Chief of the Out-patient Department for Diseases of the Eye and Ear of the Pennsylvania Hospital. Under the ear were included diseases of the nose and throat. In the report of the Hospital for the year 1880, it is stated that there were 72 new eye cases, and 33 new cases in the Department for Diseases of the Ear. Dr. Harlan remained in sole charge of the Out-patient Department for the Eye, Ear, Nose, and Throat until the year 1892, when Dr. P. N. K. Schwenk was put in as his associate in the Eye Department, and Dr. A. W. McCoy was given charge of the Department for Diseases of the Nose and Throat.

"In 1892, the last year in which Dr. Harlan did all the work himself, there were 674 new eye cases, and 522 new ear, nose, and throat cases in the Out-patient Department, an increase of over 800 new cases of eye diseases during the twelve years in which he had charge, and nearly 300 new ear, nose, and throat cases. In other words, Dr. Harlan had, by his own work, built up this large service from the very beginning.

"On April 30, 1900, Dr. Harlan was elected to the position of ophthalmic surgeon to the Hospital. . . . He rarely missed a day in his attendance upon the Out-patient Department, and he always arrived early and stayed late. During many years he did all the ophthalmic and aural operations in the wards of the hospital.

"At the time of his death Dr. Harlan was almost the oldest living ex-resident of the Pennsylvania Hospital, and during the long period in which he had been connected with it, a great number of younger men had passed through their years of residenceship in the hospital under him. His uniform kindness to the younger men of the profession, and the eagerness with which he endeavored to impart to them an understanding of the special subjects which were his province will always be a cherished remembrance of those who knew him.

"At the gatherings of the Association of Ex-residents of the Pennsylvania Hospital, no one entered more genially into the fun of the occasion, and no one will be more sorrowfully missed than their much loved senior, Dr. George C. Harlan."

The Board of Managers of the Pennsylvania Hospital, on the occasion of his resignation from the staff, on January 25, 1909, showed its appreciation of his many years of unremitting and faithful service by creating the position of emeritus surgeon, and electing him to that position.

When he resigned from the Wills Hospital, in 1901, he was made consulting surgeon and received the following minute handsomely engrossed and bound, a distinction such as had never before been conferred upon any officer of the institution:

Philadelphia, Pa. At a stated meeting of the Board of Directors of City Trusts, held May 8, 1910, the following Minute was unanimously adopted:

WHEREAS, Dr. George C. Harlan, attending surgeon of the Wills Hospital, has tendered his resignation of that office;

AND WHEREAS, Dr. Harlan has served the Wills Hospital with the utmost skill and devotion for nearly forty years, as resident surgeon in 1857, and as attending surgeon from 1861 to 1864, and again from 1868 until this time; therefore, be it

Resolved, That the resignation of Dr. Harlan be accepted with sincere regret, and that in acceptong it the Board desires to express, and preserve in its records, its appreciation of the long, faithful, and efficient service rendered by him to the Hospital and to the suffering poor of the City of Philadelphia.

LOUIS WAGNER,
President.
FRANK M. HIGHLEY,
Secretary.

Dr. Harlan was one of the oldest and most distinguished members of the American Ophthalmological Society. The high regard in which he was held by his colleagues has been thus expressed in a personal letter to the writer by Dr. Charles Stedman Bull, of New York:

"I first made the adquaintance of Dr. Harlan in 1874, at the Annual Meeting of the American Ophthalmological Society,

to which we had both been elected to membership at the previous
session, in 1873; and I was impressed by the cordiality of his
greeting and his quiet refinement of manner. It was not long
before this acquaintanceship ripened into friendship, for he was
most regular in attendance at the meetings of the Society, rarely
having missed a session during a period of over thirty years. He
had always something of interest to present for the consideration
of the members, and the presentation was always made in such a
modest manner as must have won him friends at once.

"We served for a number of years together on the Committee
on Admissions of the Society, and I was always impressed by his
courtesy of manner and his consideration for the views of his
fellow members, and by the fairness and justice of his actions.

"He was a somewhat reserved man; but as time passed, and I
reached below the surface, I soon discovered the sterling character
of the man. He was always kindly, a true gentleman at heart,
with great consideration for the feelings of others.

"He was tenacious of his opinions when once formed, but was
broad-minded and open to conviction. One strong point in his
character was his dislike of everything that smacked of sham or
pretence, and his own professional life marked the high-water
standard of his view of the ethics of his profession.

"George Harlan was a lovable man, a man of the highest
character in every relation of life; and I look back on the many
years of our unbroken friendship with a very deep regret that the
tie had been sundered by his too early death.

"His activity in the field of ophthalmology was notable. He
contributed thirty-six papers to the American Ophthalmological
Society, which have been published in their *Transactions*. These
papers cover a very wide field, and are proof of his interest in
the whole domain of Ophthalmology. In the scientific discussions
of the Society he was brief in his remarks, always spoke to the
point, and was heard with interest and respect.

"I trust that what I have written will bear testimony to the love
and respect we all have for the memory of a good man, whose loss
we all deeply feel."

Dr. O. F. Wadsworth, of Boston, another colleague of Dr. Harlan in the American Ophthalmological Society, writes of him as follows:

"At our meeting in 1875 he presented a paper on 'Two Cases of Vascular Disease of the Orbit,' with a careful, judicial review of the literature of the subject, which was of great value. From 1879 to 1902 very few meetings passed without one or more papers from him, on a large variety of subjects. He brought to the notice of the Society the Borsch spherocylindrical, toric lens, which has proved so great a boon. Whether presenting a paper of his own or discussing the communications of others, Dr. Harlan's opinion, backed, as it was, by large experience, good sense, and calm judgment, was always welcome to his colleagues and carried much weight.

"He was Vice-President of the Society from 1889 to 1893, and President from 1893 to 1898. As a presiding officer, he was quiet, dignified, and efficient; and his kindly, modest, genial disposition endeared him to his fellow members."

Dr. Harlan was elected a Fellow of the College in January, 1865. He was always most regular in his attendance, rarely having missed a meeting during a period of over forty years. He contributed many valuable papers to the TRANSACTIONS. He was one of the original members of the Section on Ophthalmology and acted as its chairman from January, 1898, to January, 1901. He was elected a member of the Library Committee on March 4, 1885, and served as chairman of that Committee from February 12, 1894, until his death. By virtue of his office he was a member of the Council from 1894 to 1909.

No Fellow of this College ever served it with greater faithfulness or more untiring zeal.

MEMOIR OF DE FOREST WILLARD, A.M., M.D., Ph.D.[1]

By ROLAND G. CURTIN, M.D.

ON March 23, 1846, a boy, the subject of this sketch, was born to Daniel H. Willard and his wife, S. Maria Deming Willard, and was named De Forest. The place of his birth was Newington, Conn., a quiet rural town about four and one-half miles from the city of Hartford. Both of his parents were descended from English strain, which upon being transplanted to New England became sturdy notable citizens, with an honorable history that anyone would be proud to possess and point to. His paternal ancestor landed in 1634, and was one of the founders of Concord, Mass. Simon Willard was a deputy for many years, and was quite celebrated as an Indian fighter; at one time he was in command of an expedition against the Niantic Indians. One author styles him as "one of the religious and courageous councillors of the ancient Massachusetts Colony." Two of Simon Willard's descendants were presidents of Harvard College, and many others could be named who have held high and important positions involving responsibility and always filling them with credit to themselves and to the satisfaction of all concerned.

At the age of eighteen months the subject of this memoir had a severe attack of poliomyelitis, which resulted in the usual shortening and atrophy with paralytic talipes varus, the latter continuing until the summer of 1864.

At the age of thirteen he entered the Hartford High School, from which he graduated with high standing at the age of seventeen. In the same spring (1863) he passed a highly creditable

[1] Read October 4, 1911.

and successful examination for entrance to Yale College, but was deterred from taking a college course owing to an impaired condition of his eyes.

Here we have briefly the history of young Willard up to the time he came to Philadelphia. His quiet rural home life in New England had given him a constitution which prepared him for his subsequent arduous work, and it also gave to him the moral straightforwardness, honesty of purpose, and thrift which characterized his future life. In September, 1863, he entered Jefferson College, where he attended medical lectures for one year.

One year after he first arrived in Philadelphia the deformity of his foot was successfully corrected by a tenotomy of the tendo Achillis, performed by Dr. D. Hayes Agnew after several of the most noted surgeons had advised against the operation. The result was markedly successful, and, taken in connection with the personal benefit derived from it, was probably what turned Dr. Willard's attention toward orthopedic surgery. It began a life-long friendship between Dr. Agnew and Dr. Willard, and further, it resulted in the latter entering the university for the end of his course. He was one of the large number of young men who received a goodly inspiration from that eminent surgeon and Christian gentleman, Dr. D. Hayes Agnew.

Dr. Willard had greatly desired entering the United States service in the Civil War, but was not eligible, being excluded by the rules laid down for the guidance of the examining surgeons. After one of the awful battles of the army of the Potomac, in the emergency, however, the United States Sanitary Commission called for volunteer surgeons and medical cadets to assist in the care of the numerous sick and wounded. This was a favorable opportunity for him to enter the service without a physical examination. He applied, was promptly accepted as an assistant surgeon, and in that capacity sent to the front, first at City Point, where he had charge of a ward and performed all the services of an acting assistant surgeon in a United States army hospital; later, he was sent to do field duty at Petersburg after the battle there, and was placed on duty at the Fair Grounds Hospital,

where later he was stricken with the low form of army typhoid, which laid him low for fourteen weeks and jeopardized his life. The weakened condition that followed this illness prevented him from continuing his medical studies until the fall of 1866. In March, 1867, he graduated from the University of Pennsylvania and was at once appointed a resident physician to the Philadelphia General Hospital, where he served with ability for fifteen months. In 1868, after leaving the hospital, he opened an office at 220 South Sixteenth Street. In 1877 the catastrophy occurred which tested his worth and metal. A brother, a widower, was drowned in saving the life of his oldest son, leaving Dr. Willard, a bachelor, with five children, the oldest of whom was only eight years of age, and the charge of a large iron forging plant near Bordentown, N. J. At this time it seemed as if his professional work must be abandoned. He boldly grappled with the task, besides practising medicine and caring for his brother's orphans, as well as running the iron business, with which he was so successful that in the sixteen years during which he had charge of his brother's estate, it doubled in value. During the first sixteen months he allowed himself only four hours' rest in bed in the twenty-four.

The subject of this memoir was possessed of an ability like Lord Palmerston, William Pitt, and Edmund Burke, to snatch at odd times a momentary "nap" under any condition and without detection. One day he was presiding over a meeting at the University of Pennsylvania. I noticed he was having a "cat-nap," in which he rhythmically nodded his head as if giving assent to the words of the speaker. This nap did not usually keep him from following the run of passing events. This ability to relax I feel sure greatly economized his strength and enabled him at this time and later to keep up with his hard, persistent work without breaking down.

He moved from 220 South Sixteenth Street to 123 South Sixteenth Street, then to 113 South Sixteenth Street, and then to 1818 Chestnut Street. In 1881 he married Miss Elizabeth Porter, daughter of Judge William A. Porter, of Philadelphia.

In 1892, after the death of his friend and adviser, Dr. D. Hayes Agnew, he purchased his house at 1601 Walnut Street, where he remained until 1900, when he sold it and returned to 1818 Chestnut Street, where he remained until his very serious illness in 1906. At this time he took up his residence at Lansdowne, Pa., a suburb of Philadelphia, at the same time having an office in the city at 1901 Chestnut Street. This arrangement continued until his death in 1910.

Soon after his graduation he began reporting the clinics for Dr. Agnew, Dr. Gross, and other surgeons. Dr. S. D. Gross, one day looking over Dr. Willard's report of one of his clinical lectures, said it was admirably done, and remarked to me that "a good report of a clinical lecture is not what the operator had said, but rather what he should have said."

Among the outside charities in which Dr. Willard was interested we may mention his long continued interest in the Aid Association of the Philadelphia County Medical Society, which is an example of his wise and persistent work for a charity that distributed its blessings annually to physicians disabled by sickness, or to the widow or fatherless families in case of death. He joined the Association October 5, 1880. It was a weak babe from poor support and with few friends. He took the Society to his own home and nursed it for years and stood by it until his death, at which time it was a lusty child. He was its President from 1890 to 1893. The fund of the Society in 1880, when he joined it, was only $400, but at the time he died it had $31,000 invested and bearing interest, which interest is being used for the benefit of medical men or their families.

In 1868, just after he graduated, he was the moving spirit in founding the Philadelphia Midnight Mission, which had for its object the rescuing of fallen women, aiding them to start a new life. He personally gained the interest of Rev. George Bringhurst and Rev. William W. Newton, Mr. W. A. Farr, and others, and they started this much needed charity, which has been instrumental in doing a very successful work. He was useful as a manager and as its physician for forty-two years.

Dr. Willard was the first one to start the hospital ambulance service in the city of Philadelphia, by presenting an ambulance to the Presbyterian Hospital. He was also instrumental in having an ordinance passed by Councils to break the line of parades in order to allow the ambulances to pass.

The Union Benevolent Association was one of the beneficial charities in which he was long interested. He became associated with the organization first as a member, then from 1883 to 1893 he was an active director.

Dr. Willard in addition to his many other outside charitable interests was a member of the Board of Managers of the Pennsylvania Training School for the Feeble Minded for many years, during most of which he was Chairman of the Medical Committee of the Board, and through his influence and untiring industry many improvements were made for the medical care of the inmates of that institution.

When the New England Society of Pennsylvania was founded, he was one of the initial coterie. At the time of his death he was the official physician of the Society.

After the death of Dr. John Ashhurst he became the patron of the John Ashhurst Surgical Society.

In 1871 he received the degree of Doctor of Philosophy from the University of Pennsylvania, and in 1889 the honorary degree of A.M. from Lafayette.

During the whole of his active professional life he taught and practised orthopedic surgery at the University of Pennsylvania, while at the Presbyterian Hospital he was a general surgeon. In 1887 he was elected lecturer on orthopedic surgery, a position that he held for about twenty years. During this time he started to organize the orthopedic work at the University Hospital.

In 1882 the Department had so grown that he saw provision must be made for a larger and more active ward. He accordingly raised the money for the establishment of the Agnew Ward for Crippled Children and supplied it with every appliance, also with a fully equipped gymnasium, where thousands of treatments are given each year. This ward was opened in 1897 and has been

constantly in active use since. With the assistance of the Ladies'
Auxiliary Committee, $180,000 have been raised for the Ortho-
pedic Department of the University of Pennsylvania Hospital
in the last twenty years. This great work was accomplished
through his instrumentality—a labor of love.

In 1889 he was elected Clinical Professor of Orthopedic Surgery
in the University of Pennsylvania. In 1893 his clinical chair
was raised to a full professorship.

When the philanthropist Mr. P. A. B. Widener decided to
found the Industrial School for Crippled Children, he consulted
Dr. Willard, who spent years and much time and thought in
carrying out the infinitesimal details of this great and novel
work; in planning buildings, appliances, course of study, and, in
fact, all the details of this magnificent charity. He watched its
progress through all the stages, and was finally rewarded by seeing
the institution formally opened in 1905, at which time he an-
nounced to those gathered there the intention of Mr. Widener to
give $2,000,000 as an endowment to the School. At this opening
it was also announced that Dr. Willard had been appointed sur-
geon-in-chief to the institution.

Dr. Willard was a faithful, untiring officer of the Philadelphia
Presbyterian Hospital, having served gratuitously in several
capacities; first as pathologist for nine years; twenty-six years as
surgeon, and for over three years as consulting surgeon.

Although a specialist in orthopedic surgery, he was eminent as
a general surgeon, and, like Dr. D. Hayes Agnew, was not only a
surgical operator but was also a worthy therapeutist.

Dr. Willard would not be classed as an ultra surgeon, but was
rather of the safe and sound progressive type, closely following
the new up-to-date ideas of the advance guard, wisely and
promptly culling the good from the bad. He did not lower his
influence by seeming indecent haste to dazzle the medical and
surgical world by much-vaunted hasty generalizations and by
crude experiments, experiments which later disproved the claims
of the originators. His advice in matters surgical was sought
often by those who knew him best, expecting a wise final decision.

He was not a promise, but an active, positive success. He won the battles of his life with credit to himself and with satisfaction to all his patients, friends, and citizens generally. This was done notwithstanding hampering difficulties which he nobly overcame. In every way he was true to his calling.

The story of Dr. Willard's career as a surgeon is the history of orthopedic surgery in America as a specialty. He was the foremost organizer and teacher, and as a practical operator he had no superior. As a writer on the subject he was always clear and concise, leaving no vague impression in the mind of the reader.

Of the four schemes that he planned for the benefit of crippled children, three have been fully carried out:

1. The orthopedic ward at the University Hospital.

2. The fund for providing orthopedic apparatus at the University Hospital

3. The great Industrial School for Crippled Children founded by Mr. P. A. B. Widener, with an endowment of several millions of dollars.

The fourth plan was for the endowment of the chair of orthopedic surgery in the University of Pennsylvania Hospital, which is yet to be carried out.

In his forty-three years of practice he accomplished much, as, for instance, the deformed children that he helped and restored to usefulness in his beneficent orthopedic work, which was enormous. Perhaps the crutches, canes, and other apparatus that were laid aside through his instrumentality might make a larger showing than those exhibited at Lourdes in France, or St. Anne de Beaupré in Canada. At these places the patients were largely, if not all, adults, while Dr. Willard's patients were generally children. Therefore, measuring the years of usefulness of his patients, it would not surprise me if Dr. Willard's benefit to the world would greatly overbalance that of the two places named.

While a resident physician at the Philadelphia General Hospital (Blockley) he joined the Presbyterian Church, and for over forty years was a constant attendant and an exemplary member thereof. He was an elder of the Second Presbyterian Church for fifteen

years and a trustee for twenty-five years, and for some years he was the efficient superintendent of the Tabor Presbyterian Church and Sunday School. He was always regular and punctual in all his religious duties and engagements. Dr. Willard was active in doing good in many ways, even outside this city and country. I may mention that at one time he was selecting a professor for the American College at Athens, Greece; at another he was assisting in the starting of a medical college in China, and again engaged in starting the Christian Settlement of the University of Pennsylvania. These were a part of his life's work, outside of medicine.

He was a man of good strong moral character, which was combined with an indomitable will and which properly directed his energies, which were entirely without any obnoxious angularities such as would detract from his usefulness or influence for good.

Dr. Willard was a man with a kind, cordial manner, having always a pleasant smile for all persons, being easily approached; the humblest charity patient and the millionaire were both received affably and cordially; all had the same kindly interest shown them. There was nothing presumptuous or vain or ostentatious in his manner, dress, or heart. He was free from all political entanglements and petty jealousies, which are so common in the medical field today and which has to some extent existed in time past. I never knew him to have a quarrel and never a serious misunderstanding with anyone.

Almost six years ago he was in his usual good health when he was invited to address the County Medical Society in Hartford, Conn. While there he was urged to give a talk to the medical men of Springfield, Mass., the next evening. He gave them a lecture and started for Philadelphia, travelling all night in order to reach home to meet his Philadelphia engagements. After trying to arrange his accumulated work he was called upon to operate upon a patient down in the Cumberland Valley below Harrisburg. Coming home late in the evening, he called upon me, as I was ill at the time. He said: "I feel the same symptoms this evening that I had when I had influenza several years ago."

A couple of hours later, at 10.30 that night, he had a chill. An attack of pleuropneumonia followed, then an empyema, which was operated upon later. Then followed nephritis, and still later, phlebitis of both lower limbs. His inheritance of the strong constitution already alluded to and a life of sobriety and regularity in his quiet domestic life enabled him to survive and largely regain his health, so that after a time he was able to attend to his office practice and the work in the Presbyterian and University Hospitals, the Widener School for Crippled Children, and to finish his book upon *The Surgery of Childhood*, the crowning act of his life, a valuable work of over 800 pages and 700 illustrations. It portrays his observation and experience in dealing with the surgical diseases of the young. He wrote many articles upon matters surgical, some three hundred being published. He de-delivered the Faculty Address at the opening of the 145th Session of the Medical Department of the University of Pennsylvania, September 23, 1910, a little less than a month before he died. In this address, which was one of high moral tone, he gave the students much good, wholesome advice. This was his last public appearance, and at its close he was weak and exhausted. Shortly after the delivery of this address he had an attack of general neuritis, followed by pneumonia, which soon culminated in death.

He made good use of all the talents that were intrusted to him and faithfully used them in the service of God and his fellow men. He had only honorable and admirable traits of character. He was pure and sincere, and his word and deed were the embodiment of honor, whether in consultation, in practice, or in his association with the laity. He always had a kind, fatherly, protecting word for his medical brethren.

In his life he had many honors showered upon or, rather, thrust upon him by his friends and admirers. These honors were not courted, but freely given as a reward of merit for good, faithful, honest work. His council, advice, and judgment were sought for and highly valued in things surgical, as well as other important matters. His influence was always for good, whether by precept or example. He was free from professional commercialism.

When he operated it was for the benefit of the patient in every way, being kind and just, no matter how poor the patient might be. It was not for his own gratification, or the fee, if any was received.

His judgment was not one of the hurried kind; he did not jump to a conclusion, nor was he a man to delay action to the harm of the patient, or until he had expired. He never swerved from duty or from truth. Measuring him up to the standard of the time, he was an able, earnest physician. His memory will be graven upon the tablets in the hearts of those who knew him well. He never sat down with folded hands, feeling that his life work was over, but worked on happily to the end. He could not stop while he was able to benefit those needing his professional care, or while humanity was suffering. He continued the battle with disease as long as he was capable of doing so. He had an instinctive love for his work.

Individuality and determined energy will often override a hindering physical deformity; for instance, Sir Walter Scott, Lord Byron, and Thaddeus Stevens, the "Great Commoner," were all lame, but triumphed over the handicap and were useful men. Dr. Willard's success in life was due to his industry, superior ability, and good judgment; when taken in connection with his Christian morality, all fitted him for his high calling.

Personally, I loved Dr. Willard for his perfect life and character, his justice, devotion, and loyalty to his family, and his life work, his friends, his colleagues, and for his charitable leniency toward those who were antagonistic to him. I knew Dr. Willard's worth, and I feel that I cannot praise him too highly. He was one of God's own sons, pure in mind and body, who has left behind him an indelible influence for good. Would that I had the power to perfectly picture to you the life of our dear departed associate. I can assure you that it would describe as perfect a life as we are privileged to see in this world. He had a purity of character, a righteous zeal, and a devotedness to his profession, a faithfulness to the service of humanity and to his friends and colleagues.

I offer this tribute to my dear friend in loving remembrance of his friendship for me, and many kind acts, all of which I now sorely miss. The epitaph that Mr. Clemens (Mark Twain) chose for his wife seems fitting for our departed fellow-member, who was just, upright, and true:

> "Warm summer sun,
> Shine kindly here;
> Warm southern wind,
> Blow softly here.
> Green sod above,
> Lie light, lie light.
> Good night, dear heart,
> Good night, good night."

PRESENTATION OF A STATUE OF ÆSCULAPIUS.

By RICHARD H. HARTE, M.D.

Mr. President and Fellows of the College:

It has been long the cherished hope of some of the Fellows of this Institution, and especially since the birth of our new building and the beginning of our new life in it, that some fitting emblematic figure should be placed on the stairway in the niche which the architects have so appropriately designed.

I feel that nothing could be more fitting in this building, which is devoted to the science and art of medicine, than a suitable statue of Asklepios, the ancient God of medical art.

Asklepios—the Greek god—who, as tradition has it, was the son of Apollo and Koronis, was born in the Valley of Hieron, about six miles from Epidaurus in the Argolic Peninsula. This Hieron was the chief seat of the worship of Asklepios, although there are many other places of minor importance, as Athens, Delphi, Troizen and others.

It was at Epidaurus that the Hieron, or Great Temple, was dedicated to Asklepios. This temple, distinctly of Greek architecture, comprised many buildings, with medicinal springs, with hot, cold, and vapor baths; also kennels for the sacred dogs and pits for the serpents, all of which played an important part in the Hieron, which really was nothing less than a large hospital, or sanatorium, where patients flocked from all parts to be relieved of various maladies.

Recent investigation and exploration have thrown much light upon this most interesting bit of archeology, and many and wonderful, we find, were the miraculous cures by Asklepios, his priests

and disciples, aided by the magic tongues of dogs and serpents. Besides the supernatural and ritualistic observances, considerable attention was devoted to diet, hygiene, and massage, interspersed with dreams, visions, incantations, etc.

Although, to our modern and scientific minds, these proceedings seem absurd, yet there are many places in the civilized world which countenance and practise rituals of much the same character, and I regret to say that many of these do not possess half the merit of the practices in vogue twenty-five hundred years ago in the Hieron of Epidaurus.

It is interesting to note that the patients whom the god cured offered him a sacrifice, usually a cock or a goat. This custom no doubt played an important part in the commissary of the Hieron, as there were always many people to be fed daily. On departure, the patient hung a tablet on the temple wall, recording his malady and the manner of its cure.

Many of these tablets have been deciphered and are of no little interest. The following are a few of them:

A man with only one eye is visited by the god in the abaton. Asklepios applies an ointment to the empty orbit. On awakening, the patient finds he is possessed of two sound eyes.

A man with a lacerated foot—the result of a bite from a wild animal—is suffering much pain. He is carried outside the abaton, a serpent comes and licks the wound, and instantly the man is cured.

Heraius, of Mytheline, suffers from baldness and applies to Asklepios, who gives him an ointment, which is applied to the scalp at night, and in the morning he is rejoiced to find that he is possessed of a good head of hair. Unfortunately, Asklepios neglected to place the prescription on the box for the benefit of later sufferers from this complaint.

Asklepios did not confine his efforts purely to the field of medicine, but dealt surgically with dropsy, in a simple but heroic manner; cutting the head from his patient, then seizing him by the feet and holding him in an inverted position until all the fluid had leaked out of the edematous body, he then replaced the

patient's head and the case terminated happily—whether in this world or another, history fails to state.

An invocation of no little interest is the following: "O blessed Asklepios, God of Healing, it is thanks to thy skill that Diophantes hopes to be relieved of this incurable, horrible gout; no longer to move like a crab; no longer to walk upon thorns, but to have a sound foot, as thou hast decreed." It is to be hoped Diophantes' desires were realized. If not, he may have regretted the premature placing of this tablet.

Not infrequently, persons with real and incurable diseases came to the Hieron and grew worse, in spite of their sacrifices and petitions to the gods. The priests were only human, and, in order to save the reputation of Asklepios, the patient was advised to seek the advice of a distant shrine, and possibly many expired on the road, thus saving the honor of the god. This interesting method has not been entirely discontinued by many of our fashionable physicians of the present day.

According to the religion of the Greeks, two events were considered to desecrate in the most dreadful way this hallowed spot, namely, birth and death; neither of these must occur in any of these sacred enclosures.

While the sick probably met with considerable kindness and humanity and real help in these shrines of Asklepios, and much actual benefit resulted, in spite of the superstition on which it was all based, still in this respect Greek tradition and ceremonies were the cause of much gross inhumanity. The unhappy patient, who was domiciled in the abaton, and whose vital powers were seen to be steadily declining, and who was, to the priests and attendants, obviously dying, instead of being tenderly nursed and soothed, was removed from his couch, dragged across the precinct to the nearest gate, expelled, and left to die on the hillside unhelped and unattended. Asklepios had rejected him, and no priest or minister of the god must defile himself by dealing with death.

A like superstition existed regarding childbirth. Many a poor woman who was anticipating maternity, and who had been hoping

for relief for some ordinary ailment, was suddenly and mercilessly expelled from the precinct at the moment when she needed help and comfort most. And it was not until the time of Antonius Pius and Marcus Aurelius that homes for the dying and a maternity hospital were erected outside of the precinct.

The Greeks displayed great judgment in selecting the sites for these temples of Asklepios. They were always located in a beautiful grove on a sloping hillside facing the south, and contained springs of medicinal virtue. With beautiful architecture, enhanced by ideal surroundings of nature, where psychopathy was practised in its most advanced form, it is not to be wondered at that the Hieron could boast of many marvellous and surprising cures which were attributed to the superhuman power of the God of the Healing Art.

There were several shrines to Asklepios situated in different parts of the then civilized world, which contained statues to the god, all varying in form, design, and importance and modified by the local traditions, according to the conceptions of the several artists who made them. A brief description, therefore, of the chryselephantine Asklepios of the Hieron of Epidaurus, which vies in beauty and importance with the great statue of Jupiter at Olympia, will not be out of place.

This great statue was constructed of ivory and gold, and represents a handsome, robust figure seated on a throne. His left hand rests on the head of a large golden serpent, and in the right hand he holds a staff, while a sacred dog lies at his right side. In this, as in various other statues of Asklepios, the face is bearded, though we learn that Dionysius, the Tyrant of Syracuse, visiting Epidaurus, stole the massive golden beard from the figure of the god. He excused the theft on the ground that it was unseemly for Asklepios to wear a beard when his father—Apollo—had none.

The usually accepted statue of Asklepios is that representing a strong, manly figure standing partly clothed in the classic tunic of the times, holding in his right hand a staff, around which is entwined a serpent—the insignia of his calling; or again, holding

in his hands a phial and staff; or at times a boy is shown standing by his side, and is supposed to be emblematic of recovery. The face is not necessarily covered with a beard, thus conforming more to the accepted type of physician of today.

The legend runs that, after Asklepios had reached manhood, reports were circulated all over the country that he not only cured the sick, but that he possessed the power of restoring life to the dead. About the manner in which he received this power there were two traditions, the one which I shall relate being the more interesting.

On one occasion Asklepios was shut up in the house of one Glaucus, whom he was to cure. While standing absorbed in thought leaning on his staff, and hardly knowing what remedy to administer, a serpent came and entwined itself around his staff. Alarmed at first, Asklepios killed it, whereupon another serpent appeared, carrying in his mouth an herb, which immediately restored life to the dead serpent. From that time, Asklepios made use of the same herb, with a similar effect upon men, restoring to life many who had died.

As the serpent, with all its *knowledge* and cunning, had been the undoing of Eve, so it happened to Asklepios; for we learn that Jupiter killed him with a flash of lightning while Asklepios was later exercising this art upon the aforesaid Glaucus, for Jupiter feared that, if these superhuman powers were not re-strained, men might gradually escape death altogether. (We read also that Plato complained that Asklepios reduced the number of the dead altogether too much.)

Mr. President, it gives me great pleasure to present to our College and its Fellows, this emblematic figure of the great science of medicine.

Our statue is an exact copy of the figure of Asklepios now in the gallery of the Vatican; of heroic proportions, as all the statues of Asklepios were so presented. Unfortunately, nearly all of them have been destroyed by the iconoclastic Christians.

It is interesting to note, in connection with this particular statue, that Augustus Caesar, who at one time had been cured

of some liver complaint by his physician, Antonius Musa, out
of respect for the latter's skill and ability, had the head of the
statue of Asklepios removed and replaced by the bust of his
favorite physician.   Musa was undoubtedly a man of great
ability, prominence, and influence in his time, as we find, upon the
death of Augustus Caesar, he was still held in great respect at the
Court of Tiberius.

Unfortunately, the scupltor is unknown, as the Roman emperors
would never permit sculptors to sign their works.

As Asklepios guarded with jealous care all through the dim
and misty ages of the past the traditions and ideals that repre-
sented medicine in those long forgotten days, may his presence
here in our beloved College be not only an ornament but an in-
centive to the Fellows, reminding them that we have had a dis-
tinguished past and, what is much more important, that a great
future lies before us, for which our honor and traditions must be
jealously watched and guarded, so that we may play our part in
the elevation and advancement of all that stands for the best in
the great field of medicine.

ACCEPTANCE OF THE STATUE.

BY S. WEIR MITCHELL, M.D.

MR. PRESIDENT AND FELLOWS OF THE COLLEGE:

I have been often honored by the Fellows of this College, but never more to my pleasure than on this occasion, when now I am asked to receive for you the generous and appropriate gift of our Treasurer, Richard H. Harte. We, Mr. President, have been so long and so well accustomed to the constancy and fidelity of service given by our officers and committees, that we may sometimes fail adequately to express ourselves for the lavish expenditure of time and thought in their official work. This devotion, this long and loyal sacrifice, has had no better exemplar than in the gentleman who now adds to this accumulated debt of gratitude a material reminder of our varied forms of obligation.

What is meant by this statue which meets our gaze as we pass through the noble hall and begin to ascend the staircase? I think it could not have been without some intention, some thought of the attributes of the "God of Medicine" here facing us, that my friend made this liberal gift and selected the place where it should stand.

It is pleasant to remember that the legend of the birth of the mythical "god of medicine" connects him with his father Apollo, the "supporter of health and the patron of literature." "In the prayers and offerings at the shrine of Æsculapius, Apollo was commonly named first, and then Æsculapius, and furthermore, according to the rule of Hippocrates, every doctor qualified as such by an oath 'in the name of Apollo the healer, and of Æsculapius, of Hygieia and Panacea, and of all the gods and all the goddesses.'"

Surely a liberal invocation for assistance in the practice of medicine. Above all, I would recall to you that this relation to Apollo seems a pledge toward those pursuits of literature which have illustrated the scientific careers of so many of the masters of medicine.

It is a pleasure to have been asked by Dr. Harte to receive for the Fellows of the College this replica of the statue of the Æsculapius of the Vatican. It is an additional pleasure, which he, I am sure, never contemplated, to have also the gratification of thanking him personally for years of admirable service, for his many gifts to the Library of the College, and for this last expression of generous interest.

We are nearing the close of four of the most brilliant years in the history of the College. Looking around me, Mr. President, I am filled with thankfulness that I have been spared to see what men like you, our Treasurer, and your colleagues of the Building Committee have here done to dignify and stimulate our profession. That profession has nowhere else such a home, and that we shall be increasingly worthy of it is my prayer and my belief. I have too the further hope that the many recent gifts to the College and this the latest and perhaps the most remarkable will lead in the future to similar instances of thoughtful giving. With all my heart, Mr. President, and for all your hearts, I am sure, I thank our Treasurer.

THE ANNUAL ADDRESS OF THE PRESIDENT.[1]

By G. E. de SCHWEINITZ, M.D.

Two years ago Dr. Tyson began his Annual Address with this sentence: "Since the reading of my last Annual Address, January 1, 1908, the interest of the Fellows of the College has largely centred in the progress of the new hall on Twenty-second Street." Progress culminated in completion, and on November 10 and 11, 1909, the new hall of the College of Physicians of Philadelphia was dedicated with impressive and dignified ceremonies, which are still fresh in the memories of those who had the good fortune to take part in them. The account of the exercises on these occasions forms part of the thirty-first volume of our TRANSACTIONS, and is further contained in a supplemental volume which, exclusive of the Fellows of the College, has been sent to each contributor of the College Building Fund.

For the success of these Dedication Ceremonies the College is indebted to the efforts of the members of the Entertainment Committee and of the Committee of Reception, and particularly to the earnest and effective work (and no one who was not actively engaged in it can properly realize how great this work was) of the Chairman of the Entertainment Committee, Dr. Charles H. Frazier.

For more than a year we, Fellows of the College, have dwelt in this new home, "of mark beyond all others," justly proud of the nobility of its structure and happily satisfied with its unrivalled equipment. It would seem proper, therefore, that this address should concern itself with the work of the College during the past year, and should review and relate those things which

[1] January 4, 1911.

have been done, those things which will be done, and those things
which ought to be done.

CONCERNING THE SCIENTIFIC BUSINESS OF THE COLLEGE.
During the last College year, *i. e.*, from December 1, 1909, to
November 30, 1910, thirty-two papers have been read at the
various stated and special meetings, an increase of seven as
compared with the scientific programs of the preceding year.
Six of these papers, two being by physicians not Fellows of the
College, were read at special meetings. Professor Magnus-Levy,
of Berlin, discoursed on "The Dietetic Treatment of Effusions
without Drugs," and his paper elicited an interesting debate.
The evening devoted to a consideration of Acute and Epidemic
Poliomyelitis was a memorable occasion, with its illuminating dis-
cussion of a disease upon which so much attention has been centred
in recent times, and for which the College is largely indebted
to the interest and activities of Dr. Charles K. Mills and to the
contributions of Dr. Paul Lewis on its etiology, of Dr. Allen
Smith on its pathology, and of the Commissioner of Health of
the Commonwealth of Pennsylvania, Dr. Dixon, through his Chief
Medical Inspector, Dr. Royer, and of the Director of Public Health
in Philadelphia, Dr. Neff, on their studies of this disease through-
out the State and city. The Postoperative Psychoses were amply
presented at one stated meeting of the College, which assumed
the character of a special session, opening with a brief and sugges-
tive paper by Dr. S. Weir Mitchell, and continuing in a scholarly
communication by Dr. Mumford, of Boston, a comprehensive
review by Dr. J. Chalmers Da Costa, and an instructive discussion
by Drs. Howard A. Kelly, Edward Martin, F. X. Dercum, C. K.
Mills, and J. K. Mitchell, the latter being especially interesting
in his analysis of his own and his father's large clinical experience.

Of the remaining papers, read at various stated meetings,
all had worthy place on the College program, but it may be
permitted to point, with special satisfaction, to Dr. Spiller's
Lantern Demonstration of Tumors of the Brain and Spinal Cord,
to a similar demonstration by Dr. Willson of the Gross Pathology
of the Heart, to Dr. Stengel's contribution on the Treatment of
Acute Pulmonary Edema, to Dr. Hare's studies in Pneumonia
and the Differences between Systolic Blood Pressure in the Arm

and Leg in Aortic Regurgitation, and to Drs. Pemberton's and Sweet's experiments relating to the Induction of Pancreatic Activity by Removal of the Adrenals.

The average attendance of the Fellows during the stated meetings of the College was practically 69 (exactly $68\frac{3}{9}$), an increase of over 11 above that of the preceding year, while the attendance of the Fellows at the special meetings averaged practically 64. All of these special meetings devoted to scientific subjects, however, were well attended by physicians who are not Fellows, and the officers of the College have received many expressions—not only from Fellows, but from physicians in the city and its immediate neighborhood—of satisfaction that these important subjects were brought forward, and that opportunity was given to those who are not members of our institution to hear the papers and to take part in the proceedings.

The Public Lectures on "Great Doctors and Achievements in Medical Research," inaugurated by the College at the suggestion of Dr. S. Weir Mitchell at the January meeting, have been a pronounced success. On each occasion a brilliant audience greeted the lecturer, and those who attended will not soon forget the pleasure and profit which Dr. Mitchell's delightful lecture on "Harvey and the Circulation of the Blood," Dr. Flexner's scholarly account of "Pasteur and the Rise of Modern Bacteriology," and Dr. Welch's characteristically charming talk on "Jenner and Vaccination" afforded them. Invitations to these lectures were mailed not only to each Fellow of the College and to all members of the County Medical Society, but also, issued from the President's office, to more than thirteen hundred prominent men and women resident in this city and its neighborhood. Through the *Weekly Roster* a general invitation was sent to all physicians in regular standing in Philadelphia. These lectures have not only served, as it was intended that they should, to educate the public, but they have also served, in a perfectly proper manner, to focus as never before in our history the attention of the citizens of this municipality upon the College and its worth, work, and influence, so that they have come to realize how important our institution is and how well it deserves their interest and support.

As the result of a conference between Dr. Alfred Stengel, Dr. A. O. J. Kelly, and the President, and with the permission of the College, granted at its May meeting, the Weir Mitchell Lectures have been established, the first one of which will take place during the present month, as already announced, and be given by the Professor of Pharmacology in the University of London, Arthur R. Cushny, and the second one by Edmund B. Wilson, Professor of Zoölogy in Columbia University, the subject and date of which will be published later. During the remainder of the year two and possibly three additional lectures will be given. It is the hope of the Committee that a sufficient fund will be available, from the income of which a suitable honorarium can be paid to each lecturer, and, while he will not be forbidden to utilize his material for publication in some medical journal, that it will also form part of the yearly volume of the TRANSACTIONS OF THE COLLEGE OF PHYSICIANS. With the interest of the Fellows in bringing to the College meetings their best efforts, with the continuance of the Public Lectures, and with the success which promises to be attendant on the Weir Mitchell Lectures, the special committee which has them in charge, as well as the Committee on Scientific Business of the College, confidently believe that the scientific program of the College for the coming year will not only equal that of the past, but excel it. For what has been done in this respect I desire to express the College's and my own high appreciation of the work of the Committee on Scientific Business of our institution, and particularly of that of its efficient Chairman, Dr. A. O. J. Kelly.

The Publication Committee is to be congratulated upon the material contained in the last volume of our TRANSACTIONS, and it is fortunate that this Committee was able to print with the other papers Professor Martin H. Fischer's essay on "Edema," to which the 1909 Nathan Lewis Hatfield Prize of the College of Physicians was awarded. If happily in future it should be possible to include some or all of the Weir Mitchell Lectures, to which I have made reference, as well as the more important papers read before the Sections of the College, our TRANSACTIONS will grow in importance and reach a point of distinction they

have never before attained, and yearly constitute better than ever real additions to the literature of our profession.

CONCERNING THE LIBRARY. The report of the Library Committee, presented by its Chairman at the last meeting of the College, leaves little for me to add, and what I say must in large part be a repetition and an emphasis of some of its salient points.

The total number of volumes in the library at the present time is 91,673. Of unbound theses and dissertations we possess 24,967, and of unbound pamphlets, 79,676. From all sources the library has acquired during the last year 4146 volumes, 14,791 pamphlets, and 36,924 numbers of various periodicals. It is interesting to note that of the 678 new publications added to the library during the past year, 42 were written or edited by Fellows of the College.

Certain changes in the conduct of the library instituted by the Library Committee have been of special satisfaction to the Fellows—namely, improvement in the rapidity with which the books are bound, thus obviating the inconvenience of long absences of sample copies from the library shelves; permission to use ink by the readers and workers in the library, and the opening of the library on two nights a week and on certain legal holidays other than Christmas, New Year's Day, Thanksgiving Day, and Fourth of July. Now, while it is true that the use of the library at night has been limited to about fifteen Fellows, and that the total average attendance was only about five, and for actual Fellows of the College about half of this number, this does not represent a discouraging record. In the first place, what I may call the habit of consulting the library at night requires some time before it is acquired, and in the second place, the Fellows who have made use of the privilege are especially those whose active literary work in subsequent publications or in Society discussions adds to the reputation of our institution and its collegiate body.

Of particular value have been the seminar rooms, and to quote from the report of the Chairman of the Library Committee, "they have been highly appreciated by the Fellows of the College, inasmuch as the majority of them have been in use all the time and all of them for the greater part of the year. The number

of volumes called for and retained in these rooms for use has averaged about fifty the year round."

This is the first entire year that the library has occupied its new quarters, and in spite of the fact that the number of hours were increased during the summer and that the library was kept open on minor legal holidays, and at night for two evenings each week from March 2, except from June 15 to September 15, there was a decrease in the number of visitors when compared with the last full year that the library occupied its old quarters at Thirteenth and Locust Streets. During this last full year at Thirteenth and Locust Streets, namely, during 1908, 12,166 visitors were recorded, of which, 6491 were Fellows of the College; in other words, nearly one-third more readers and visitors were present than during the year which has just ended. It seems to me that this difference is readily explained: (1) It is due to the change in location, an influence which was to be expected during the first year and which will steadily decline, and (2) it was natural that in the last year of our residence in the old quarters an unusual number of Fellows and visitors should be attracted to the College, partly in farewell visits, and partly because it was a common ground, for the discussion of subjects in which the College was vitally interested. This is indicated if a comparison is made between the attendance during this year and that of the preceding year, namely, 1907, which shows an increase during 1908 of more than 5000 all told, and of more than 3000 Fellows of the College. If, now, a comparison is made between the number of visitors and Fellows registered during this year of 1907, and during the year just ended, we find that the increase is over 1000 in favor of the new building.

The library funds have been increased during the last year by the generous gift of Dr. Francis X. Dercum, of $5000, and by that of Mrs. Henry Swords, of $1000, to found the Gerardus Clarkson Library Fund. The total investment at the present time is $72,332.57, the annual income from which, amounting to about $3292.94, is used for the purchase of new publications and for subscriptions to periodicals, the income of the George B. Wood Fund, amounting to somewhat over $300, being utilized for library supplies.

CONCERNING GIFTS TO THE COLLEGE. At the February meeting Dr. John K. Mitchell, in the absence of Dr. S. Weir Mitchell, read the following letter: "I have this great pleasure, to give to the College of Physicians of Philadelphia $75,000, to relieve it from debt and leave it free to pursue its career of honorable usefulness." Signed, Edward T. Stotesbury. This act of Mr. Stotesbury places his name high on the roll of eminent benefactors of the College, but it does more than this, it makes him a conspicuous benefactor of the medical profession at large, and establishes an example of generosity which it is fondly hoped will be emulated by other public-spirited citizens.

To the generous additions to the Library Fund reference has already been made, and the following is a list of the rare medical books, works of special interest, paintings, engravings, statuary, and other valuable gifts received by the College during the past year.

Incunabula. (Total number, 151.)

Cerasianus, J. Repetitio sententiam sanguinis. Leipzig, Lotter, 1499.
Fiera Mantuanus, S. Cœna seu de cibariorum. Venetiis, de Boll, 1485.
    (Presented by Dr. George Fales Baker.)

Works of Special Interest.

Brissot, P. Apologetica. Parisiis, Colinesei, 1525.
Calvin, J. Defensio orthodoxæ. Oliua, Stephani, 1554
    (Presented by Drs. S. Weir Mitchell, W. W. Keen, R. H. Harte, and
    J. G. Clark.)
de Clementinus, C. Clementia medicinæ. Roma, Mazochius, 1512.
Fabricius ab Aquapendente, H. Opera chirurgica. Patavii, Matthacide
Cardorinis, 1666.
    (Presented by Dr. S. Weir Mitchell.)
Fallopius, G. Opera omnia. Francofurti, Wicheli, 1600.
    (Presented by Dr. Barton Cooke Hirst.)
von Gerssdorff, H. Feldtbuch der Wundarztney. Strassburg, Schott, 1517.
    (Presented by Dr. George W. Norris.)
Hippocrates. Magni coacæ prænotiones. Parisiorum, Meturas, 1658.
    (Presented by Dr. Francis R. Packard.)
Original Drawings and Letters of Joseph Leidy, M.D.
    (Presented by Dr. J. Willcox through Dr. W. W. Keen.)
Mesue Damascenus, J. Mesue vulgar. Venetiis, Arrivabeno, 1521.
Morgagni, G. B. Autograph letter to S. F. Morand, 1750.
    (Presented by Dr. John H. Musser.)

Rhases. Opera parva. Lyons, de Villiers, 1510–1511.
Servetus, M. De trinitatis erroribus. Basle, Koenig, 1531.
    (Presented by Drs. S. Weir Mitchell, W. W. Keen, R. H. Harte, and
      J. G. Clark.)
Tokumoto. Bikwa mujiujo. Kioto, 1766.
    (Presented by Dr. Albert S. Ashmead.)

Oil Paintings.

Portrait of Dr. Nathaniel C. Chapman, by Sully.
    (Presented by Mrs. Henry C. Chapman.)
Portrait of Dr. Adam Kuhn, by Louis Hasselbusch.
    (Presented by C. Hartman Kuhn, Esq.)
Portrait of Dr. Arthur V. Meigs, by William M. Chase.

Busts.

Marble bust of Dr. S. Weir Mitchell, with pedestal, by Partridge.
    (Presented by Mrs. S. Weir Mitchell.)
Marble bust of Æsculapius, with pedestal.
    (Presented by Dr. John B. Roberts.)
Marble bust of Dr. George B. Wood.
    (Presented by Messrs. Craige, Walter, and J. Bertram Lippincott.)
Bronze bust of Dr. Horatio C. Wood, by S. Murray.
    (Presented by Messrs. George Wood and George Wood Bacon.)

Medals.

Bronze medal commemorative of the dedication of the new building of the
College of Physicians of Philadelphia.
    (Presented by Dr. James Tyson.)

Framed Pictures, Diplomas, etc.

Proof before letters of S. Medley's painting of the President, Fellows, and
Corresponding Members of the Medical Society of London. Engraved by
N. Branwhite.
    (Presented by Hampton L. Carson, Esq.)
Silhouettes of Dr. John Redman, Dr. Samuel Powell Griffitts, and Dr.
Abraham Chovet.
    (Presented by Hampton L. Carson, Esq.)
Copy of Harvey's Stemma. Painted by Mrs. J. M. Taylor.
    (Presented by Dr. S. Weir Mitchell.)
The Island of the Tiber, which, for nearly twelve hundred years, was conse-
crated to the Spirit of Healing.
    (Photographed and Presented by William Romaine Newbold.)
Diploma of honorary membership given to David Grove by the Royal
Jennerian Society, May 12, 1832.
    (Presented by Dr. Roland G. Curtin.)

Gold watch, formerly owned by Dr. D. Hayes Agnew.
    (Presented by Dr. Henry D. Jump.)

To only a few of these gifts is it possible for me to make reference in the present address. Our incunabula, now numbering 151, have been increased through the generosity of Dr. George Fales Baker, and represent a notable collection and compare favorably with those owned by the great libraries of Europe. Our art gallery has been enriched by the portrait of Dr. Nathaniel C. Chapman, a fine Sully, presented by Mrs. Henry C. Chapman; by one of Dr. Adam Kuhn, presented by Mr. C. Hartman Kuhn; by one of our honored former President, Dr. Arthur V. Meigs; and by one of Dr. Joseph Parrish, presented by Mrs. Susan Parrish Wharton. In the coming months admirable portraits of the late Dr. William Goodell and of Dr. James Tyson will be presented, and soon thereafter a portrait of our late Vice-President, Dr. Wharton Sinkler, and one of Dr. George C. Harlan.

To Dr. John B. Roberts we are indebted for a marble bust of Æsculapius; to Messrs. Craige, Walter, and J. Bertram Lippincott for a marble bust of Dr. George B. Wood; to Messrs. George Wood and George Wood Bacon for a bronze bust of Dr. Horatio C. Wood; and to Mrs. S. Weir Mitchell for the splendid marble bust of Dr. S. Weir Mitchell, which so fittingly stands in this the great Hall of the College of Physicians, named for, and dedicated to, our most distinguished and beloved Fellow.

In the near future, as the College has already heard, through the interest of Dr. Abbe, of New York, we will, under certain conditions already presented to the College, become the custodians of the watch of Dr. Benjamin Rush.

CONCERNING THE BUSINESS TRANSACTIONS OF THE COLLEGE. In March of the last year the President of the College was approached by the officers of the Free Library of Philadelphia with an offer to lease the property at Thirteenth and Locust Streets. The Committee in charge of the disposal of these properties (Dr. J. C. Wilson, Dr. Richard H. Harte, Dr. John B. Roberts, and the President), after a thorough investigation of this matter, in consultation with Mr. Frank P. Prichard, recommended at a special meeting of the College, held on February 4, 1910, that a lease should be drawn on the following terms: Beginning July 1, 1910, for five years, the rental was to be $7000 per annum,

and the lessees are to pay all taxes, water rent, insurance, repairs, municipal improvements, etc., and indemnify the College against all charges of every kind against the property, the lessees to have the privilege of renewal on proper notice for another five years, year by year, with an increase of $700 during each year of renewal. These eminently satisfactory terms were approved by the College at the special meeting before mentioned, and the lease was signed on February 28, 1910.

In February of last year the President ascertained that the stable and the three small houses adjoining the College on the south had passed into the possession of a firm of real estate agents, whose plans included the erection of a garage. Largely through the efforts of one of our Fellows, Dr. James Thorington, the owners of these properties offered to sell them to the College for $46,000, which was $4000 less than the original price asked, and $7000 less than the price which they said they would ask after they had acquired the property. A very short time was given to the College in which to decide the matter, and to meet the demand of a $16,000 payment in cash, $1000 upon execution of agreement, and the balance of $15,000 within five weeks from the date thereof. How to avoid this difficulty, and how to come into possession of these properties in the absence of any funds belonging to the College which could be properly utilized for such a purpose, was indeed a problem, solved by the devoted interest of our well-beloved late Vice-President, Dr. Wharton Sinkler, whose touching interest in this matter, extending almost to his dying day, can never be forgotten. Through his influence his nephew, Mr. Eckley B. Coxe, Jr., purchased the property, with the understanding that while the College was in no sense obliged to take it from his hands, he was ready at any time to place the College in possession of these buildings and lots under the most liberal terms. This was the announcement that the President of the College was able to make at the meeting of March 2, 1910, to the infinite relief and great satisfaction of all Fellows of the College.

Subsequently, with the active interest and help of Mr. Charles Sinkler, Mr. Coxe offered to convey these premises to the College for a cash payment of between $5000 and $6000, that is, such

an amount as reimbursed him over and above $40,000, reserving a ground rent of $1600 a year, or 4 per cent. on $40,000.

By a resolution of the College at its May meeting, 1910, the Committee in charge of this matter was empowered to purchase the stable property adjoining the College on the south side under the conditions named to the President, briefly as follows: That at the settlement Mr. Coxe will pay the first mortgage of $20,000, will receive a ground rent of $40,000, leaving approximately $5250 to be paid. Under date of June 22, Mr. Prichard, the attorney for the College, sent to the President of the College the deed in duplicate from Mr. Eckley B. Coxe, Jr., with the request that both copies be signed by the President and Secretary of the College and the seal of the College attached. Proper acknowledgment was made by the Secretary of the College before the Notary in Mr. Prichard's office, and the matter was concluded. Settlement took place on July 1, Mr. Evans, of Mr. Prichard's office, attending, who represented the College, and later the President of the College received from Mr. Sinkler the various memoranda of settlement.

At the October meeting of the College the action of the officers in purchasing the property was ratified by a resolution which also confirmed the execution of the deed of ground rent upon the property.

The stable, therefore, has passed into the possession of the College, and the rents from the stable and from one of the houses at the rear of the stable, as long as it existed, in part reimbursed the College for its payment on the ground rent. Owing to the unsanitary condition of these small houses, it was agreed that they should be torn down and the lot properly protected with a fence. The expiration of the lease on the stable does not take place until June of this year, giving the College, it would seem, ample time to determine what disposition shall be made of this property after this lease expires. To this point I shall return in a later portion of this Address.

The high appreciation in which the College holds Mr. Coxe's generosity in this matter has been emphasized by a vote of thanks, which has been formally conveyed to him.

The College has heard the remarkably satisfactory report

which the Hall Committee has been able to present, by which it seems that the calculated minimum expenditure for the year was reduced by about $500, a feat in economy and efficiency which, as the Chairman of the Hall Committee, Dr. John K. Mitchell, has pointed out, is due to the constant personal effort and attention of every member of his Committee, as well as to the effective work of the Superintendent of the College, Mr. Fisher, and the Clerk of the College, Miss Zelner.

Reference must here also be made to the report of the Building Committee, presented by its secretary, Dr. William J. Taylor. This Committee, under various resolutions adopted by the College, was authorized to expend upon the erection and furnishing of the new building a sum not to exceed $295,000. At the date of this report, namely, November, 1910, $293,809.89 had been expended, leaving a balance, therefore, of $1190.11. In addition to this, certain special funds have been provided for furnishing the various named rooms of the College to the amount of $14,832.31, and for these beautiful and fitting memorials we are indebted in the Cadwalader room to Mrs. S. Weir Mitchell; in the Thomson room to the children, nephews, and nieces of the late Dr. William Thomson; in the Ashhurst room to Dr. Richard H. Harte; in the Norris room to the sons and some of the relatives and friends of the late Dr. William F. Norris; in the Wood room to the Wood family; in the Packard room to the brothers of the late Dr. Frederick Packard; in Mitchell Hall to the generosity of many friends and Fellows of the College, and particularly to the untiring activity of Dr. John H. Musser; and in the Hutchinson Reception Room to the descendants of Dr. James Hutchinson and to the family of the late Dr. James H. Hutchinson.

The Fellows of the College have learned from the report of our Treasurer that the income from the invested funds for the year 1911 will be practically the same as for 1910, namely, $8319.45; that the income from real estate will be approximately $7437.50, and that the income from annual contributions for the year 1911 will amount to about $12,150, making a total of $27,906.95, or somewhat over $7000 more than the income of the College in the year which has just ended, the increase being due to the rental received from the old buildings at

Thirteenth and Locust Streets. The Finance Committee has appropriated the necessary funds for the various departments of the College, and these appropriations have been made in as liberal a spirit as possible. A good working balance remains, not by any means more than we need, but more than we dared to hope would be available before we were relieved of the burden of indebtedness by the generous gift to which I have already made reference.

The satisfaction which has resulted from the improved business methods of the College, whereby a trained bookkeeper in the Treasurer's office handles all accounts, except those of the Mütter Museum, which is operated according to the provisions of its deed of trust, must be evident to all of the Fellows. Moreover, the care and fidelity with which the Superintendent of the College has performed his duties has added not a little to the success which has crowned our efforts during the last year, and my distinguished predecessor may well be pleased that the suggestions which came from him in these respects have proved to be of such great advantage to the College.

At the meeting of December, 1909, the College adopted a resolution that the officers of the College be empowered to have prepared and presented to the court through counsel a petition asking for permission to increase the amount of property that may be legally held under the charter. Through the agency of Mr. Frank P. Prichard the petition was duly made and a decree of court has been granted increasing the limit of the holdings to $200,000. All business brought to the attention of the College from the Council, from reports of special committees, and from resolutions presented on the floor of the College, has been duly and I believe satisfactorily transacted, save only that the appointment of a committee, authorized at the February meeting, to take into consideration the means to abate the coal smoke nuisance in Philadelphia, was not formed, because after consultation with the Director of Public Health, himself a Fellow of the College and keenly interested in the success of the movement, it was plain that for the present more effective work in this respect would come through other channels. In the near future the

College, it is hoped, will take further steps in this matter and will be ready to do its part in this civic duty.

CONCERNING THOSE WHO HAVE DIED DURING THE YEAR. The last year, rich as it has been in the joy of successful achievement, has not been free from sorrow. Against the names of seven of the Fellows of the College "the fatal asterisk of death is set."

Dr. William B. Stanton, elected a Fellow in 1904, died on February 13, 1910. An accomplished clinician, splendidly active in the tuberculosis work of the city and of the State, distinguished for his studies in cardiovascular disease and for his invention of one of the most accurate instruments for its detection, he represented the best type of physician and was a real inspiration to those who knew him and worked with him.

Dr. Wharton Sinkler, elected a Fellow in 1872, died on March 16, 1910. Through all the years of his Fellowship he was devoted to the best interests of the College, rendering special service in its Committee on the Directory for Nurses and in the Council, and becoming its Vice-President in 1910. It is difficult to realize that his fine career has come to an end, hard to believe we have lost the inspiration of his vigorous presence and the benefits of his cheerful activities. A real doctor, there was healing in his touch; an acute clinician, there was wisdom in the records of his observation; a loyal friend, there was more than comfort in his kindly offices, so often and so graciously tendered. The memory of him and of that which he accomplished remains a precious possession.

Dr. Barton H. Potts, elected a Fellow in 1902, died on May 8, 1910. An accomplished laryngologist and aurist, he was earnest in his work and successful in his results, giving, in so far as this College is concerned, valuable attention to the development and improvement of its Section on Otology and Laryngology.

Dr. D. F. Woods, elected a Fellow in 1866, died on July 28, 1910. A busy and successful practitioner in the best sense of that term, and for many years effectively interested in the work of the Presbyterian Hospital, he is greatly missed by those who depended on him for comfort and advice in their hour of need.

Dr. Walter F. Atlee, elected a Fellow in 1857, died August 18,

1910, and therefore a member of our Fellowship for more than fifty years. Quietly interested in the scientific side of our profession, and keeping in touch with European ideas by virtue of membership in foreign societies, lending his rich experience as consultant in one hospital and visiting physician in another, he was for many years a man greatly concerned with a large and important practice, to the needs of which he administered with conspicuous ability. Kind to the poor, he was also kind and helpful to the younger members of the profession, to whom words of encouragement from one of his large influence always mean much.

Dr. De Forest Willard, elected a Fellow in 1880, died October 14, 1910. A noted surgeon, conspicuous for his work in orthopedic surgery and the surgery of children, a teacher of distinction, for many years holding the chair of orthopedic surgery in the University of Pennsylvania, and in largest measure responsible for its fine orthopedic department, liberal in his contributions to the literature of his special branch of our science, he was a man of the highest ideals and of the best influence, and was a real exemplar among the members of our profession.

Dr. James B. Walker, elected a Fellow in 1885, died October 18, 1910. For many years meeting cheerfully and skilfully the exactions of a large and influential practice, he none the less found time to be notably active in the affairs of the State and of the County Society, serving both in positions of the highest importance, and to contribute to the literature of medicine from his rich clinical experience. Always prompt to respond to the call of friend or patient as the need arose, his ministrations brought comfort to many households and his death a sorrow not easily assuaged.

Thus, the College has lost by death during the year seven Fellows. One Fellow has resigned, and one Fellowship has been forfeited. Twenty-four new Fellows have been elected. The net gain, therefore, is fifteen. On December 1, 1910, the roll of the College was as follows: Fellows, 451; Associate Fellows (American), 26; Associate Fellows (foreign), 20; corresponding members, 4; a total of 501.

CONCERNING THOSE THINGS WHICH OUGHT TO BE DONE. Practically two-thirds of the present income of the library is

used for periodical publications and one-third for new books. It is desirable that a larger income shall be available for the purchase of books and journals, for binding, and for the care of our most notable possession. The citizens of Philadelphia have come to know what a valuable library we have, and, moreover, that it is a free library, containing many volumes that are of the greatest interest to those who are not medical men. I urge that each Fellow shall make it his business to present the claims of the College in this respect to those who are likely to respond to appeals for aid, and to remember a sentence from an address of Dr. S. Weir Mitchell, which reads as follows: "It may chance to some of you to be able to enlist in favor of the library outside aid from those who have the good habit of giving."

Reprints of the Annual Report of the Library are distributed to the medical libraries of the world and to representative medical journals in all countries. Now, while this report states the facts, it is a comparatively small pamphlet, and is not as large as the Annual Report of the Honorary Librarian to the Library Committee. It does not, in my opinion, or in the opinion of the Librarian, represent as fully as it should the affairs of such an important institution as is the College of Physicians. The reports issued from other libraries, for example in Boston and New York, are larger, and include not only matter which pertains especially to the book collections, but other records of interest connected with the institutions from which they proceed. It would seem, therefore, proper to recommend that this report shall be elaborated, and that it shall hereafter contain, for example, the President's Annual Address, and such data as may with advantage be abstracted from the Report of the Honorary Librarian, making special reference to books of unusual interest or great value. This surely would result in a report which would make a much better impression than the one which now proceeds from the offices of the College.

Our collection of incunabula and old books is now a notable one, and as Dr. Keen has suggested and urged, it should be the endeavor of all those interested in our library to increase it, either by gift or purchase, or by the raising of a fund from the income of which volumes of this character can be purchased.

It is, moreover, exceedingly desirable that a catalogue of our incunabula shall be constructed, which can be sent, as is the Report of the Library Committee, to the various great libraries of the world. We are fortunate in that the post of Honorary Librarian of this College is held by one who is so well qualified to undertake this work, and to whom, I trust, this recommendation will appeal.

The satisfaction with which the announcement of the establishment of the Weir Mitchell Lectures has been received, and that we are to have in the College of Physicians the opportunity of hearing distinguished lecturers at stated intervals, exactly as they are heard in New York under the auspices of the Harvey Society, makes me bold to urge on the Fellows the necessity of endeavoring to raise a fund, from the income of which a proper honorarium may be paid to each lecturer. We should have at least $10,000 for this purpose, and while I know of some contributions that have been made, and have faith that others will follow, I cannot resist the opportunity of presenting the financial needs of this important departure in our affairs. Each step which advances the scientific output of this College is of advantage not alone to the profession at large, but to the city, whose reputation is thus enhanced. Such a fund is, therefore, a perfectly proper object of appeal which I hope will not be neglected.

Our unsightly surroundings are gradually disappearing, and with the termination of the lease of the stable this building will be razed to the ground and our most objectionable neighbor removed. When this is accomplished I venture to hope that some memorial will arise to him to whom we are most indebted for this happy relief, our late Vice-President and well-loved Fellow, Dr. Wharton Sinkler.

In this address, which of necessity has been longer than is usual on this occasion, I have called attention to some of the possessions of the College, but I have made no reference to that which is our most valued asset, namely, the fine spirit which pervades this collegiate body in that each Fellow yields to it a cheerful loyalty and unselfish service which are real inspirations in the work that we are doing and an earnest of the things which we shall do.

THE QUANTITATIVE DETERMINATION OF FUNCTIONAL RENAL SUFFICIENCY BY THE DUBOSCQ COLORIMETER; INDIGOCARMINE VERSUS PHENOLSULPHONEPHTHALEIN.[1]

A PRELIMINARY REPORT.

By B. A. THOMAS, M.D.,

PROFESSOR OF GENITO-URINARY SURGERY IN THE POLYCLINIC HOSPITAL AND COLLEGE FOR GRADUATES IN MEDICINE, PHILADELPHIA.

(From the William Pepper Laboratory of Clinical Medicine.)

IT is conceded that the most reliable individual kidney test is one dependent upon a quantitative metabolic study. By reason of the complicated conditions entailed, the requirement of particular physiologico-chemical knowledge, and the consumption of time demanded for the completion of the necessary observation, which even then may not be conclusive, as von Noorden has demonstrated, such a procedure is destined never to become popular. Indeed, the mere fact that every four or five years witnesses the announcement of a new method for determining the kidney function suffices to prove (1) that the old tests are inadequate or unsatisfactory, and (2) that it still remains the keen concern not only of the internist, but particularly of the surgeon, to find some test, whereby the health or disease of the kidney may conveniently be determined.

Various drugs and dyes have been utilized in countless attempts to solve this perplexing problem, in the subcutaneous employment of which attention has been directed to the time of onset of their elimination by the kidneys, to the constancy of reaction, and to the intensity, maximum, and duration of their excretion. Attempts

[1] Read February 1, 1911.

to compute the quantitative elimination of these substances have never, until recently, been crowned with notable successes. Formerly, with methylene blue, in order to determine the amount of the dye excreted, the colored urine was measured and placed in a glass container. Precisely the same quantity of water was placed in another glass, and known quantities of methylene blue added until the two solutions became homogeneous in coloration. The percentage of the aniline dye eliminated in the urine was then easily and approximately computed.

During the past year Rowntree and Geraghty have called attention to the great advantages of phenolsulphonephthalein, a substance first described by Ira Remsen, for a functional renal test, placing especial emphasis upon the quantitative estimation of the percentage of the drug eliminated by the kidney during the first hour or two following its injection subcutaneously.

The structural formula of this phthalein may be represented as follows:

$$C \underset{\underset{SO_2}{\diagdown \diagup}}{\overset{C_6H_4 \quad O}{\diagdown \diagup}} \diagup C \diagdown \overset{C_6H_4OH}{\underset{C_6H_4OH}{}}$$
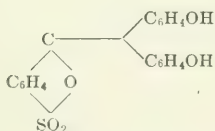
This substance is a bright red, crystalline powder, slightly soluble in water, but more so in alcohol; insoluble in ether; in dilute alkaline solution it is a purer red than phenolphthalein, being purple in strongly alkaline solution.

This phthalein has certain properties not possessed by phenolphthalein which recommends it highly in work on the physiology of the kidneys. It has a stronger avidity as an acid and is much more completely eliminated by the kidney than phenolphthalein. It may be administered by mouth and subcutaneously without ill effect. Employed more accurately by the latter method in doses of 6 mg. to the cubic centimeter, it is absolutely non-irritating, devoid of toxicity, and appears in the urine in normal individuals in about ten minutes. It is also excreted in the bile, only to be reabsorbed, however, in the intestinal tract.

Phenolsulphonephthalein is unquestionably one of the very best substances at our command for purposes of functional renal diagnosis and prognosis. The test is very delicate, and, as is the case with phloridzin, it may prove to be oversensitive. Owing to the small quantity of the drug required for injection, which produces no pain or tenderness, it can be highly recommended to the internist for use in very sick and nervous patients, in whom it is desired to estimate the total renal function, but for unilateral diagnosis, the grave concern of the surgeon, it is extremely doubtful whether phenolsulphonephthalein can ever supplant indigocarmine.[1] The latter, although not eliminated so extensively by the kidney, has not yet been shown to be inferior to phenolsulphonephthalein as a quantitative functional test. It seems unfortunate that two such meritorious tests must be brought into comparison. It would be better, perhaps, if we were to differentiate the subjects suitable for the application of either, because in unilateral diagnosis indigo will suffice to meet the demand in cases impossible of ureteral catheterization, where the phthalein test must necessarily fail.

The technique of the phenolsulphonephthalein test is as follows: Fifteen minutes to half an hour before administering the test the patient is requested to drink two glasses of water to insure free renal activity. One c.c. containing 6 mg. of the phthalein is injected subcutaneously.[2] If it is desired simply to learn the total kidney sufficiency, as may be the case in the various forms of nephritis, or the extent of renal drainage due to vis à tergo pressure, atrophy of the parenchyma of the organs, etc., because of obstruction in the lower urinary tract, as by prostatic enlargement, etc., a catheter is introduced into the bladder and the onset of the excretion of the phthalein noted by the beautiful amethyst-red produced when it comes in contact with the drop or two of 25 per cent. sodium hydroxide placed in the bottom of the receptacle used for collection. The

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[1] For description and technique for employment of this dye in functional kidney diagnosis, see author's articles, Chromocystoscopy in Functional Renal Diagnosis, Based upon the Employment of Indigocarmine, Surg., Gyn., and Obstet., April, 1909, or Penna. Med. Jour., September, 1909; Ueber die Chromoureteroskopie in der funktionellen Nierendiagnostik, Zeit. f. Urologie, May, 1911; or The Value of Chromoureteroscopy in Functional Kidney Diagnosis. Surg., Gyn., and Obstet., April, 1911.

[2] This substance is prepared by Hynson, Westcott & Co., Baltimore, Md.

quantities of urine for the first and second, or possibly third, hours are then collected. Instead of the procedure by catheterization, at first continuously and then hourly, the patient may be requested to void voluntarily every five minutes until the onset is observed, and then at hourly intervals. Such a procedure is simplicity itself, but not more so than the indigocarmine technique. On the contrary, if it be desired to determine the functional activity of the individual kidneys separately, an act is demanded which may be, and not infrequently is, impossible, namely, catheterization of one or both ureters, in order to convey the phthaleinized acid urine externally to an alkaline medium, so as to study the color reaction. With indigocarmine, catheterization of the ureters is rarely necessary, since the onset of the indigo elimination can be readily seen through the cystoscope as the blue jets of urine are ejected from the ureteral orifices into the bladder. Indeed, from an analysis of over one hundred cases subjected to the indigo test, the time of onset runs a close parallel to the quantity eliminated, and judging alone from the time and character of the elimination, in no instance has a false prognosis relative to renal sufficiency or insufficiency been made.

It has been alleged against indigocarmine that it does not lend itself well to colorimetric determinations. It is claimed that the urinary constituents cause a decomposition of the dye. With this statement I cannot agree, and believe that indigo is as efficient as the phthalein for colorimetric readings.

It is indisputable that for certain kidney conditions quantitative determinations are most valuable, whether the substance employed be indigocarmine, phenolsulphonephthalein or what not. During the past year or two Oppenheimer and Rowntree and Geraghty have employed the Duboscq colorimeter with gratifying success for the estimation of renal activity, and the last two in particular are very high in their praise of the instrument.

As shown in the figures, the Duboscq colorimeter consists of two glass cylinders, T, T, cut with parallel plane surfaces placed on arms capable of vertical movement by the manipulation of set screws on the posterior surface of the instrument. These crystals may be raised

and lowered in glass reservoirs containing solutions, the comparative colors of which are to be determined. In one reservoir, R, is placed the standardized solution; in the other, L, the solution to be tested. The mirror M is adjusted so as to reflect light through the perforated stage, S, into the reservoirs supported by the same, thence to the glass parallelopipeds P and P'', and so through the telescope to
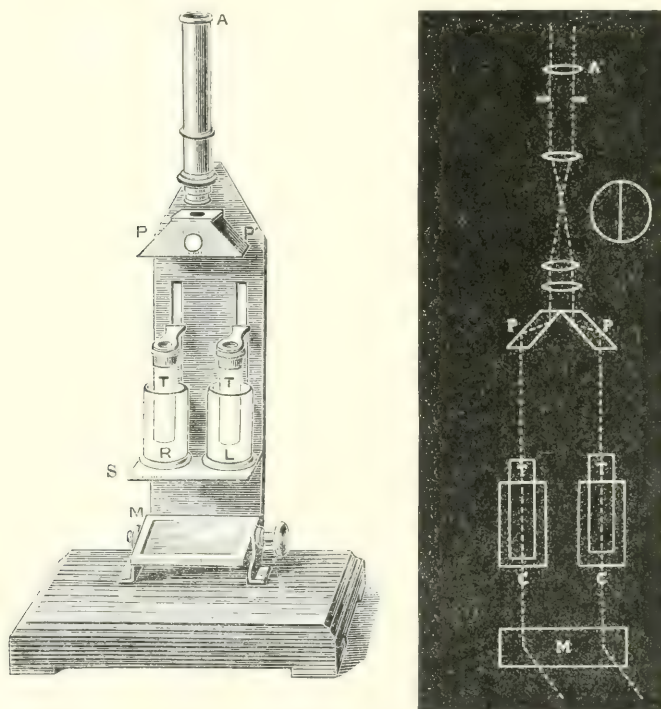
Duboscq colorimeter.

the ocular A. By manipulation of the set screws the crystals are elevated or lowered until a homogeneous coloration appears at the ocular. Scales, with Vernier attachments, invisible in the figures, furnish the readings from which the percentage of color in the solution to be tested can be computed.

In the performance of the colorimetric test, 0.5 c.c., containing

3 mg. of phenolsulphonephthalein[1] is placed in a flask and diluted up to 1000 c.c., adding one drop of 25 per cent. sodium hydroxide to elicit the amethystine coloration. This can be preserved indefinitely for future determinations. The reservoir R is then about one-half filled with this control solution and the plunger lowered until the index on the scale reads 20. This reading is arbitrary, as any other may do. Within a few minutes following the subcutaneous injection of the patient with 1 c.c. or 6 mg. of the phthalein, it begins to be eliminated in the urine, occurring normally in the acid state as an orange yellow. This may be collected by voluntary urinations, by urethral catheterization, or by ureteral catheters if the work of the kidneys individually is desired. The onset of elimination is determined by collecting the urine in the presence of a drop or two of the sodium hydrate solution, noting the occurrence of the pinkish color. Quantitatively, the amounts of the first and second hours are collected separately. Each amount is rendered definitely alkaline by the addition of sodium hydrate, and is diluted up to 1000 c.c. A quantity of this is filtered and placed in the reservoir L. The left hand set-screw is then manipulated until a similar coloration is observed on both sides, and the reading taken. If, for example, the reading on the left is found to be 40, and, as previously stated, the control reads 20, it is obvious that the solution to be tested is only half the concentration of the control, which may be graphically represented as follows: $\frac{20}{40} \times 100 = 50$ per cent. Inasmuch as the control is made up of but one-half in the case of phenolsulphonephthalein, and only one-quarter in the case of indigocarmine, of the amount injected into the patient, it is necessary in the former instance to divide the result by two and in the latter by four in order to determine the actual percentage eliminated of the amount injected into the patient.

The Duboscq colorimeter is an ideal instrument for quantitative colorimetric determinations, not only by virtue of the simplicity of its construction, but also because of the accuracy of results ob-

[1] If indigocarmine is used, 5 c.c. of a 0.4 per cent. solution is placed in the flask for the preparation of the control solution. It will be noted that only a fractional part—in the case of the phthalein one-half and with indigo one-fourth —of the amount administered to the patient is employed in the control. This is done because the solutions in these dilutions lend themselves more favorably to colorimetric readings.

tained by its use. A review of Table I will demonstrate the close parallelism existing between the findings with this instrument as compared with known solutions of indigo and phthalein.

TABLE I.—Solutions in Distilled Water.

No.	Known quantity of indigocarmine.	Amount estimated.	Known quantity of phenolsulphonephthalein.	Amount estimated.
1	0.0014 gram	0.0013 gram	0.0027 gram	0.0028 gram
2	0.0039 "	0.0039 "	0.0023 "	0.0024 "
3	0.0029 "	0.0028 "	0.0037 "	0.0037 "
4	0.0056 "	0.0057 "	0.0042 "	0.0043 "
5	0.0053 "	0.0052 "	0.0055 "	0.0055 "
6	0.0071 "	0.0071 "	0.0074 "	0.0074 "
7	0.0065 "	0.0065 "	0.0089 "	0.0088 "
8	0.0087 "	0.0086 "	0.0087 "	0.0087 "
9	0.0078 "	0.0078 "	0.0095 "	0.0095 "
10	0.0093 "	0.0094 "	0.0098 "	0.0098 '

That quantitative colorimetric determinations of indigocarmine and phenolsulphonephthalein in functional kidney diagnosis are of great value is undisputed. Whether or not the quantitative estimation will in time supersede in value the onset of elimination is a mooted question and to my mind a very doubtful one, save for the determination of the total renal function particularly for the purposes of the internist. There can be little doubt that in certain conditions, as nephritis, and especially in prostatic enlargement, where, as a rule, the kidneys are more or less damaged by a vis à'tergo pressure from retained urine, the colorimetric determinations are of exceptional value, and I confidently believe that every surgeon contemplating prostatectomy will not only decrease his mortality, but will also avoid debasing the profession of medicine, by refusing to operate in such cases when the total output for the first hour of indigo and phthalein falls below 10 and 20 per cent. respectively. I have long since been convinced that an onset of the elimination of indigo after twenty minutes bespeaks renal insufficiency and contraindicates operative interference. Again, it must be borne in mind that even though the quantitative elimination is found to be below the figures above stated, operation may be considered, provided the elimination during repeated determinations remains constant, evidencing no tendency to fall, thereby establishing a stable kidney activity. On the contrary, an operation undertaken in the presence of a steadily decreasing functional capacity, as measured

most accurately and satisfactorily by colorimetric determinations, is little short of criminal, as the patient will invariably die.

An important field which should be studied, relative to the quantitative elimination of indigo or phthalein, is that of all operative cases. It is quite possible that by an analysis of several hundred cases thus tested by these substances before operation, data might be derived that would in the future lower the general surgical mortality.

The problem that I hope to solve eventually—as I do not think the results of the cases analyzed to date sufficiently conclusive—is the determination of the relative merits of indigocarmine and phenol-sulphonephthalein. In order to accomplish this I have undertaken comparative studies of the action of both substances on a series of dogs and patients. It was at first attempted to study the onset of elimination of both substances from the ureteral orifices into the bladder of large female dogs by cystoscopy. The procedure was difficult, owing to the fact that the etherized dog seemed able to retain very little fluid in the bladder in the presence of the cystoscope. It was also very evident that the anesthetic (ether) markedly diminished the excretion of urine and, in one case at least, produced anuria. In the dogs subjected to indigocarmine the fluid used for distending the bladder was water; in those injected with phenol-sulphonephthalein the fluid employed was 25 per cent. sodium hydrate. In no case was indigo or phthalein eliminated from the ureteral orifices for forty-five minutes. At the termination of that period the dogs were allowed to revive from the anesthetic. The two dogs injected with indigo immediately voided a faintly blue-colored urine; one dog having received phthalein voided at the end of an hour, the urine demonstrating the presence of that drug; the fourth dog refused to urinate. The results are tabulated below:

TABLE II.—Dogs Cystoscoped.

No.	Substances used in tests.		Appearance of drug by cystoscopy, under ether.	Onset of secretion subsequently.
	Indigo.	Phthalein.		
1	20 c.c. of 0.4 %	. .	0	45 minutes.
2	20 c.c. of 0.4%	. . . . . .	0	45 minutes.
3	. . . .	1 c.c. = 6 mg.	0	60 minutes.
4		1 c.c. = 6 mg.	0	

Owing to the poor success of the first attempt, it was decided to perform ureterotomies under ether in the second series, catheterizing the ureters and collecting the respective urines, both for onset of elimination and quantitative study. The results are noted in Table III.

TABLE III.—Dogs Operated Upon.

No.	Substances used in tests.		Onset in minutes.		Quantitative determinations.						
	Indigo.	Phthalein.	Right ureter.	Left ureter.	First hour.		Second hour.		Third hour.		Total.
					Right ureter.	Left ureter.	Right ureter.	Left ureter.	Right ureter.	Left ureter.	
1	40 c.c. of 0.4%	..	5	5	1.63%	1.03%	1.37%	0.51%	1.48%	0.64%	6.66%
2	40 c.c. of 0.4%	....	45	45	......	......	trace	0.29%	......	......	0.29%
3	......	2 c.c. = 12 mg.	0	0	0	0	0	0	......	......	Nil
4	....	2 c.c. = 12 mg.	15	15	1.35%	2.41%	trace	1.32%	0	0.35%	5.43%

Judging from the few dogs thus far utilized, there would seem to be slight preference in favor of indigocarmine. By multiplying the number of experiments with dogs, I hope eventually to throw some light on this important problem, although it is not improbable that the human subject will suffice to settle the dispute.

In Table IV are tabulated a number of cases, normal and diseased, that have been subjected to the indigocarmine and phenolsulphonephthalein tests. In a few instances comparative applications of both methods for as many as four hours have been made.

It will be observed from a review of the tabulated cases, although too few in number for absolute conclusion, that the onset of elimination of both indigo and phthalein runs a close parallelism with the quantitative output; that as substances for quantitative determination in the estimation of renal sufficiency, they are essentially equal in value; that both substances are largely eliminated during the first two hours after injection; that the percentage output of indigo is approximately about one-half that of phthalein, which fact, however, is of no moment in drawing conclusions; that in normal ambulatory cases the onset occurs in about ten minutes, while the total output exceeds 60 per cent. of the amount injected; that in

contradistinction to the ambulatory cases, the bedridden patients, even though possessing supposedly normal kidneys, excrete less than one-half of the amount eliminated by the cases at liberty to move about, and finally, that the output of indigo occurs slightly earlier and continues no longer than the phthalein.

CONCLUSIONS. 1. Quantitative colorimetric determinations of indigocarmine and phenolsulphonephthalein are of very great value in the estimation of the total renal function, particularly in such conditions as nephritis and damaged kidneys, incident to prostatic enlargement, etc., causing poor drainage and resulting in vis à tergo pressure. These substances routinely employed by the surgeon as indicators for or against surgical intervention, particularly in contemplated prostatectomies, but likewise in other fields of surgery, will aid materially in the reduction of operative mortality.

2. Although each substance has its particular advantages and indications as a test, indigocarmine, at least for the purposes of the surgeon, especially in the diagnosis and prognosis of unilateral renal disease, seems just as useful and possibly more practical than the new drug phenolsulphonephthalein.

3. Phenolsulphonephthalein in many respects is an ideal substance for employment in studying the pathology and physiology of the kidney. It may possibly be more sensitive than indigocarmine; in fact, may prove to be too delicate. On the other hand, the technique of the test is extremely simple and may be employed painlessly. Preference should be extended to this drug over indigocarmine whenever it is desirable to learn the total or combined efficiency of both kidneys.

In conclusion, I desire to express my grateful appreciation to Drs. Edsall, Frazier, Riesman, and T. T. Thomas for permitting me to use material that made it possible to conduct, in part, these studies.

TABLE IV.—Quantitative Colorimetric Tests on Human Beings.

Normal Cases.

Name.	Diagnosis.	Indigocarmin. Amount injected.	Onset. R	Onset. L	1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Phenolsulphonephthalein. Amount injected.	Onset. R	Onset. L	1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Urinalysis and Remarks.
L. S.	Normal (ambulatory)	8 mg.	Before 10 min.		11.84%	4.86%	1.75%	0.91%	19.36%	6 mg.	Before 10 min.		37.59%	23.69%	9.62%	...	70.9%	Negative.
I. G. G.	Normal (ambulatory)	8 mg.	Before 9 min.		10.86%	8.44%	2.06%	1.01%	22.37%	6 mg.	Before 9 min.		58.47%	6.28%	3.62%	1.4%	69.77%	Negative.
Z.	Normal (ambulatory)		.....		...	...	...	...	?	6 mg.	Before 15 min.		33.44%	18.66%	5.62%	4.32%	62.04%	Negative.
B. A. T.	Normal (ambulatory)	8 mg.	5 min.		7.53%	?	2.56%	1.44%	?	6 mg.	Before 9 min.		30.12%	18.38%	13.58%	3.76%	65.84%	Negative.

Abnormal Cases.

Name.	Diagnosis.	Indigocarmin. Amount injected.	Onset. R	Onset. L	1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Phenolsulphonephthalein. Amount injected.	Onset. R	Onset. L	1 hr.	2 hrs.	3 hrs.	4 hrs.	Total.	Urinalysis and Remarks.
R. C.	Nephrolithiasis (Rt.) (bedridden)	8 mg.	10 min.	7 min.	3.35%	5.47%	1.35%	0.51%	10.68%	6 mg.	18 min.		11.00%	6.95%	3.22%	1.89%	23.06%	Urine: negative save for few erythrocytes. (Calculus 1 cm. in diameter removed.)
W. E.	Myocarditis (bedridden)	8 mg.	9½ min.	9½ min.	10.82%	2.07%	...	...	12.89%	6 mg.	?		5.91%	21.36%	...	...	27.27%	Urine: Acid, 1012, faint trace of albumin, hyaline and light granular casts, cylindroids, mucus. Blood pressure {Sys. =185, Dias. =125}
M. K.	Nephritis, interstitial, chronic (bedridden)	8 mg.	13 min. feeble	0 in 30 min.	0.90%	0.86%	...	...	1.76%	6 mg.			...	...	...	...	...	Urine: Acid, 1009, cloud of albumin, hyaline and light granular casts, cylindroids, leukocytes. Blood pressure {Sys. =220, Dias. =125}
J. S.	Nephritis; tuberculosis, pulmon. (bedridden)	8 mg.	9 min.	9 min.	4.03%	6.49%	...	...	10.52%	6 mg.	No elimination for a period of two hours.							Urine: Acid, 1019, cloud of albumin, many hyaline and light granular casts, few erythrocytes, mucus. Blood pressure {Sys. = 125, Dias. 80}
C. O.	Prostatic hypertrophy; cardiorenal disease (bedridden)	8 mg.	15 min.	15 min.	6.25%	1.56%	...	...	7.81%	6 mg.	20 min.		7.22%	9.61%	...	...	16.83%	Urine: Acid, 1015, faint trace of albumin, few hyaline and granular casts, few red blood cells and white blood cells. Blood pressure {Sys. =165, Dias. 105}
H. R.	Nephritis, hemorrhagic? (bedridden)	8 mg.	11 min.	12½ min.	?	?	...	...	2.04%	6 mg.			...	...	...	...	...	Ureteral Catheterized Specimens: Acid, 1015, heavy cloud of albumin, leukocytes and pus cells, erythrocytes, bacteria, no casts.

	Diagnosis			Dose	Time					Total	Urine / Notes
N. A.	Diabetes mellitus (bedridden)			6 mg.	15 min.	2.61%	23.07%	trace		25.68%	Sugar -6.25%.
J. McD.	Endocarditis (bedridden)			6 mg.	Earlier than 40, not at 20 min.	3.1%	9.04%	10.12%	?	13.87% 22.26%	Urine: Acid, 1028, large amount of albumin, pus, hyaline and granular casts, cylindroids. Lost cardiac compensation.
B. O.	Nephritis, parenchymatous, chronic (bedridden)			6 mg.	12 min.	10.80%	9.35%	2.8%		22.95%	Urine: Acid, 1021, albumin = 9 pro mille (Esbach), many hyaline, light and dark granular casts, colloid casts, many white blood cells. Blood pressure {Sys. =140 Dias. =120
D. W.	Nephritis, interstitial, chronic (bedridden)			6 mg.	....	1.61% 2.77%	9.34% 11.95%	5.26% 18.56%		16 21% 33.28%	Urine: Alkaline, 1018, trace of albumin, few hyaline and granular casts, few erythrocytes. Blood pressure {Sys. =235 Dias. =150
R. C.	Fracture, compound; amputation of leg; (bedridden)			6 mg.	?	3.11%	1.28%	0		4.39%	Urine: Cloud of albumin, few cylindroids, leukocytes in excess.
J. J.	Lymphadenectomy (bedridden)			6 mg.	11 min.	22.83%	5.18%	trace		28.01%	Urine: Acid, 1023, faint trace of albumin, hyaline and light granular casts, many cylindroids, mucus, excess of leukocytes.
H. S.	Tuberculosis, hip (bedridden)			6 mg.	59 min.	21.36%	?	1.06%		22.42%	Urine: Alkaline, 1008, faint trace of albumin, few polynuclear granular casts, few cylindroids, leukocytes, erythrocytes.
G. P.	Varicocele, postoperative (bedridden)			6 mg.	30 min.	14.04%	10.57%	1.01%		25.62%	Urine: Alkaline, 1022, faint trace of albumin, normal leukocytes, epithelium.
I. B.	Tuberculosis, os calcis, (bedridden)			6 mg.	20 min.	30.03%	1.59%	trace		31.62%	Urine: Acid, 1021, few hyaline casts, cylindroids, leukocytes in excess, mucus.
F. W.	Wound, gunshot, spine; monoplegia (bedridden)			6 mg.	12 min.	12.72%	1.12%			13.84%	Urine: Alkaline, 1026, faint trace of albumin, mucus.
H. J.	Tuberculosis, spine; psoas abscesses; amyloid kidneys? (bedridden)			6 mg.	29 min.	trace	0			trace	Urine: Acid, 1017, trace of albumin, hyaline, dark and light granular casts, normal leukocytes, mucus.

DISCUSSION.

Dr. James Tyson: We are very much indebted to Dr. Thomas for bringing our attention to this method of determining the sufficiency of the kidneys. The term "sufficiency of the kidney" has been used for a great many years without any very definite knowledge as to what constitutes it. The secretion of a normal quantity of urine containing the normal quantity of the varying constituents of the urine has been until recently the only means by which we could ascertain the function of the kidney, except by the grave accidents which determine it too late.

As the Fellows of the College will have noted, the practical application of this test is for the most part entirely satisfactory in determining the propriety of operation. In medical diagnosis there would be also an application of it, although of less practical value. It is well known that in the contracted kidney, for example, elimination is very much delayed, and that in parenchymatous degeneration of the kidney it is more prompt. This is confirmed by the color tests. The methylene blue sometime ago suggested is a rough method of diagnosis based on the same principle and one which is well sustained by the morbid anatomy. The method presented by Dr. Thomas has the advantage over the use of methylene blue seemingly in the painlessness of the injections. The injection of methylene blue is quite painful and its administration by the mouth unsatisfactory.

It is interesting to recall that these methods of determining the sufficiency of the kidney have failed to take hold of the internist to the degree which one would suppose they might. It is to the credit of the surgeons and to the discredit of physicians that the latter have not availed themselves as much as they might have done of these tests, and I believe that a little more careful, systematic, and prolonged study of the application of these color tests would help the internist as well as the surgeons. Of course, the conditions are somewhat different. It is well known that surgical operations are dangerous when there are kidney complications, and the information that is furnished by such a test as to the sufficiency of the kidney is a valuable guide to the operator. In medicine, if it is thus determined that an insufficiency exists, efforts can be made to increase the elimination by the ordinary channels. I think advantage would come to us in a more general application of the knowledge thus obtained.

Dr. George Erety Shoemaker: One point which has contributed to the practical value in these color tests is the development of the cystoscope. Ingenious mechanical improvements have added much to what

can be seen and done through these instruments, but the elaborate ones, while having a wider range, are too big, or have a special tip which for mechanical reasons will often bring just a little blood. Surgeons have wisely feared to traumatize the ureter, the urethra, the bladder of the patient who was suffering from infection or disease. The development of the very small perfectly smooth magnifying cystoscope added to this color test makes it possible without anesthesia and without traumatism to watch very readily the activity of the kidneys as contrasted one with the other or with a normal standard. Dr. Thomas is to be congratulated upon his presentation of this subject and upon his patient work in this promising field.

DR. A. O. J. KELLY: I have been much interested in this presentation from several points of view, and notably from the point of view of the physician with regard to the quantitative test of the renal capacity of the kidney as compared with the methods now used. As the elimination of these colors represents an effort on the part of the kidney to eliminate some foreign substance, are we justified, from delayed elimination, in assuming that the kidney is insufficient. It would be of interest if the younger surgeons would give us some idea of the relative advantage of color tests as compared with the ordinary methods. It sometimes happens that a man of middle age or beyond is in a condition which needs some surgical intervention, the removal of the prostate, or other operation requiring anesthesia. As far as it is possible to determine, his renal functions prior to the operation are normal. Repeatedly such patients, within twenty-four or thirty-six hours after operation, die with more or less renal complications. Is it possible in such a case to determine by the color test whether the renal capacity is below par, or are we justified in assuming that the retention of the color is a sign of insufficiency. This is of importance to physicians as contrasted with surgeons. Perhaps we shall learn something more about it if Dr. Thomas and others continue their studies.

DR. THOMAS, closes: In reply to Dr. Kelly, I alluded in my paper to the fact that I was continuing the study with reference to renal deficiency in conditions of prostatic hypertrophy and nephritis. There are many other surgical conditions in which there is disease *en masse* of the organs where indigocarmine is of value. In those conditions of nephritis and prostatic enlargement resulting in damage to the kidneys it is a fact already established, although perhaps too little known, that the elimination of these substances, the aniline dye and the phthalein, runs a more or less parallelism with the physical and chemical findings of the urine. In the table it will be observed that there are a number of cases presented in which the test has been employed associated with the urin-

alyses and blood pressures in these patients.   There is a close relationship
and it is remarkable that the color tests promise much of value in the
field of urological diagnosis.

In reference to Dr. Tyson's statement that the methylene blue and
these tests are not new ideas, it may be noted that methylene blue origi-
nated as a test in 1897 in the experiments of Achard and Castaigne, and
fell into disuse because, as pointed out by the Germans, the substance
possessed the following faults: Inconstancy of color reaction, polycyclic
curve of elimination, and the fact that at times it was eliminated as a
colorless chromogen.

Indigocarmin, strongly advocated by Völcher and Josef in 1903,
is always eliminated as a constant color and also more profusely than
methylene blue. It possesses a monocyclic curve of elimination, and
promises to be much more enduring in its value.

Phenolsulphonephthalein, first recommended within the last ten months,
is a substance having nothing to do with the aniline dye class, being a
drug or phthalein.   Consequently the folly of relegating it to the class of
methylene blue in valuation, or, for that matter, indigocarmine, which
has proved itself in every way far superior to the older dye.

MALPOSITIONS OF THE COLON, WITH SPECIAL REFERENCE TO THEIR CONGENITAL ORIGIN.[1]

By FLOYD E. KEENE, M.D.

THE formerly neglected symptom, constipation, has within recent years assumed important proportions, and in tracing its etiology, mechanical factors have been found to underlie many cases previously ascribed to habit, faulty innervation, etc. The colon as the chief offender in the production of chronic constipation has been a favorite field of investigation. Were we to accept the statements of a Metchnikoff or a Lane, practically all the ills of the human race could be traced to this portion of the bowel as the source of evil. While these zealous enthusiasts have probably magnified their results through the glass of their hobby, it is undoubtedly true that colonic stasis exerts a deleterious influence upon its bearer, and that it forms the underlying condition in many patients who are cast aside with the deplorable diagnosis neurasthenia.

A thorough understanding of the various forms of constipation presupposes an intimate knowledge of the anatomy, physiology, chemistry, and pathology of the gastro-intestinal tract. My province this evening has to do only with a brief discussion of that form due to mechanical obstruction secondary to malicious angulations of the colon.

Considered from the standpoint of surgical intervention for the relief of these cases, the word ptosis has been unfortunately chosen, especially as applied to the transverse colon and sigmoid flexure, which are subject to great variations in size and position. It is undoubtedly true that many operative failures have been

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[1] Read March 1, 1911.

due to partial excision or suspension of what was considered an abnormally low transverse colon or redundant sigmoid, leaving unaltered the true underlying cause, viz., a sharp angulation. In other words, the colonic length *per se* has little or nothing to do primarily with the production of fecal stasis. This statement has been proved clinically many times. The primary cause lies in a vicious position of the colon, producing angulation. In the presence of this angulation a partial obstruction of the fecal current results, with overloading of that portion of the colon proximal to the obstruction, and it is then that its redundancy acts secondarily.

These angulations are by no means limited to any one segment of the colon; furthermore, they may exist singly or in combination. The colonic topography varies so markedly in these individuals that a careful study of each case is necessary to determine the site of trouble. Not infrequently the greatly dilated cecum occupies the pelvis; due to its dependent position and weakened musculature, the cecum becomes loaded with feces, and, dragging on the terminal portion of the ileum with its short mesentery, causes a partial obstruction at or near the ileocecal junction. Again the cecum may have undergone incomplete decensus, or it may exhibit an axial rotation, the appendix lying behind or to the outer side, with sufficient distortion of the ileum, which must follow this rotation to retard the normal evacuation of its contents. The position and angulation of the flexures depend largely upon the extent and strength of peritoneal fusion during the stage of development. The splenic flexure and descending colon are fairly constant in their position and fixation, while the hepatic flexure and ascending colon are subject to the widest variations. The ascending colon may be supplied in part or throughout its whole length with a mesentery, leading to a complete obliteration of the hepatic flexure and permitting that portion of the colon which should have been the transverse to reach the high splenic flexure at a sharp angle through a series of conglomerate coils. Close coaptation of the limbs of the splenic flexure may lead to firm union by adhesions which still further accentuate the angle.

In even more exaggerated cases the entire colon possesses a long mesentery, under which circumstance all semblance of normal outline is lost and numerous distortions almost completely block the lumen. Likewise the sigmoid flexure presents various conformations which permit angulation at one or the other of its fixed extremities or along its course. One often observes firm adhesions on the outer surface of the mesosigmoid which by their contraction produce kinking. According to Lane, these bands, which are also found in other localities, are evolutionary, Nature's effort to overcome undue mobility. While primarily intended to be beneficial, their further development may prove prejudicial by producing overcorrection with obstruction.

The foregoing is but a brief summary of the gross anomalies commonly observed at the operating table. A better appreciation of these variations will be afforded by the photographs which Dr. Ginsburg has obtained in the dissecting room.

Through my association with Dr. Clark, it has been my privilege to observe a large number of these cases from both the clinical and operative viewpoint. Almost invariably the patient presents the history of life-long constipation. The associated characteristic train of symptoms may have existed for years or may be of more recent origin, dating from childbirth, trauma, or lingering illness. With this symptomatology in mind in conjunction with the findings at operation, which could be unsatisfactorily explained on an acquired basis, I undertook a series of autopsies on babies in the hope of determining a possible relationship between the conditions existing during early life and those found in the adult. Before mentioning these findings, let us review briefly the embryology of the gastro-intestinal canal.

The gastro-intestinal canal consists primarily of a straight tube closely attached to the primitive posterior abdominal wall. Very early a portion of the upper segment shows a bulging posteriorly and a concavity anteriorly, corresponding to the future greater and lesser curvatures of the stomach. As a result of the increasing volume of the liver and the increased length of the stomach segment, there is a rotation to the right, so that what

was originally the left side has become the anterior surface, and the right side the posterior surface of the fully developed stomach. Early in fetal life the size of the liver is out of all proportion to that of the abdominal cavity. Consequently the rapidly increasing length of the intestine demands more room for its development. In order to find space, it passes out of the abdominal cavity through the umbilicus, where it remains for some time. As a result of this migration, an anteroposterior U-loop is formed, consisting of a proximal descending and a distal ascending limb. As these limbs increase in length they approach one another, and later an axial rotation of the loop takes place, so that the lower limb passes over the upper. While both limbs increase in length, this takes place more rapidly in that portion which is to become the small intestine, viz., the original upper limb. Mall has demonstrated that while the intestine lies extra-abdominally, the small intestine arranges itself into six primary coils, which in their future growth become more complex, but nevertheless can be definitely outlined in the adult.

As the result of this axial rotation referred to, the small intestine assumes a position below and to the left of the large intestine, which is now an inverted U-shape and extends anteroposteriorly to the midline of the posterior abdominal wall. Later, a rapid increase in the size of the abdominal cavity permits the intestine to reënter. According to Mall the upper portion of the small intestine first assumes its position in the left hypochondriac region, to be followed by the remainder of the small intestine and the colon, the cecum returning last. The coils which were at first arranged vertically now assume a transverse position.

In early fetal life the cecum develops as a small bud from the beginning of the ascending limb. The appendix at first comes from its tip like the handle of a funnel, but as the result of the unequal growth of the anterior and right walls the appendix is thrown posteriorly and to the left.

On reëntering the abdomen, the colon retains its inverted U-shape, but the upper limb of the U is pushed transversely by the small intestine below and the stomach and liver above, the cecum lying just beneath the liver. The colon continues to increase in

length after birth, and with this growth there is a migration of the cecum downward into the right iliac fossa with the formation of the ascending colon. This does not take place completely until some time after birth. At birth the sigmoid forms a large portion of the colon and is an intra-abdominal organ; not until the third year of life do the adult proportions obtain. While originally the entire colon is supplied with a mesentery, by a process of peritoneal fusion the ascending and descending colons are deprived of a meson.

Summarizing the observations which I have made in 25 autopsies, we find that during early infancy the colon is subject to marked variations in size, extent of fixation, and position. At birth the cecum occupies a high position, but even by the end of a few months has assumed its normal position in the right iliac region or has descended into the pelvis to such an extent that its tip lies on the left side. Premature peritoneal fusion or other anomalies may hinder proper descensus or may produce other distortions of the cecum and ascending colon. The transverse colon usually occupies the upper portion of the abdomen, assuming numerous and irregular plications to accommodate itself to its narrow confines. Even in infants of approximately the same age its length varies between wide limits. This likewise applies to the sigmoid, which is proportionately largest at birth. The splenic flexure is fairly constant in its position; the hepatic flexure varies considerably. In the light of these observations, together with the clinical history so often associated with these malformations, we may be warranted in assuming the following conclusions:

1. The primary cause of vicious angulation productive of chronic constipation lies in some developmental abnormality of the colon.

2. These angulations may be active from the earliest months of life, or a faulty mechanism may perform its work normally until some extraneous cause, such as childbirth, lingering illness, or trauma, converts what may be termed a potential angulation into an actual obstruction by disturbing the intra-abdominal equilibrium, which permits sagging of the intestine with the formation of kinks at the junction of a fixed and movable segment.

A CONSIDERATION OF THE ANATOMICAL RELATIONS OF THE GUT TUBE.[1]

By NATHANIEL GINSBURG, M.D.

THE development of the mature intestinal tract from the primitive gut tube offers one of the most interesting anatomical instances of visceral rearrangement in the morphological development of the human organism. The prevailing views regarding the changes which the intestinal tube exhibits during its growth were very materially altered by the careful studies in reconstructions made by Mall. To him we owe much of our later and more accurate knowledge concerning the early relations of the primary U-shape loop of intestine, which finally by developmental changes results in the topographical relationships of the intestinal tube, as we ordinarily observe it at birth or shortly after. A knowledge of the changes in position, length, and diameter, incident to the development of the digestive tube, is imperative to properly appreciate any departures from the normal, whether they be regarded as defects in development, anomalies, or "disharmonies of nature."

The early fetal arrangement of the six primary coils of the small intestine and the position of the large bowel are not of accidental or chance occurrence. They are the result of certain definite

forces on the part of nature, which have for their specific purpose
the topographical establishment of the gut tube as it is observed
at birth. For instance, the position assumed by the duodenum is
dependent upon two factors: (1) The degree of rotation of the
stomach on its longitudinal axis, and its migration to a transverse
position in the upper abdomen. (2) This portion of the small
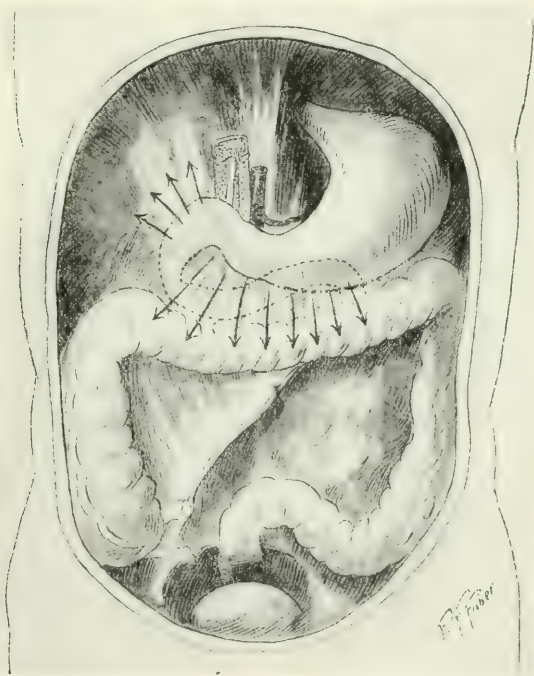
Fig. 1.—Direction of forces acting on shape of duodenum. The cardiac and pyloric portions
of the stomach represent fixed points.

intestine is pushed into a retroperitoneal position on the anterior
surfaces of the lumbar vertebræ, owing to the early anterior and
horizontal position which the transverse colon assumes in the
upper abdomen.

These two factors largely determine the topography and shape
of the duodenum. Imperfect drainage or partial occlusion of this

part of the gut tube, unless of pathological cause, is usually the result of anomalous development.

The ascending, transverse, and descending portions of the colon owe their various relationships in the abdomen to the disproportionate development of the small intestine. The overgrowth of this segment of the gut tube pushes the ascending and descending
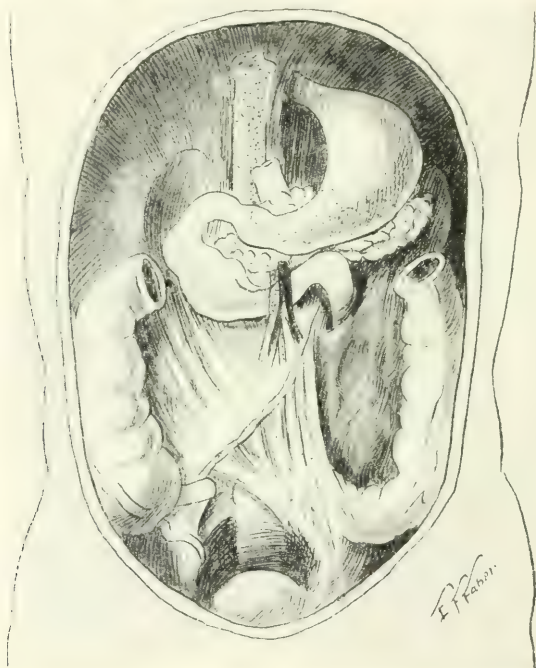
FIG. 2.—Relation of superior mesenteric artery to ventral surface of duodenum. Sigmoid tied down by bands passing to under surface of mesentery.

portions of the colon dorsolaterally, and causes the transverse colon to assume a ventrosuperior position. Arrested development affecting any part of the large bowel or its mesentery is usually the underlying cause of anomalies in arrangement and position. The mere fact that the sigmoid colon at birth is nearly one-half of the entire length of the large bowel is explanatory of

the amazing variations in length encountered in my own exami-
nations of this particular segment of the bowel.

Continued study of variations affecting one or many parts of the
large or small intestine is certainly convincing of the fact that many
so-called postgenital anomalies are only exaggerated anatomical
defects whose underlying causes are of developmental origin.
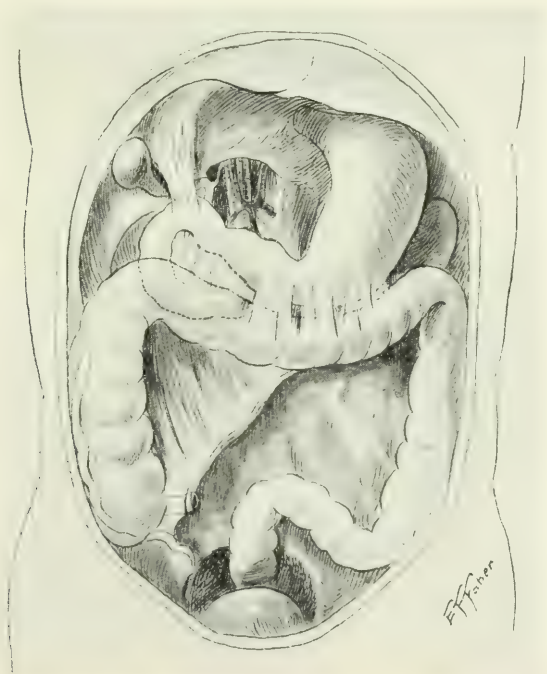
Fig. 3.—Stomach fixed by esophagus and hepaticoduodenal ligament.   Traction on greater
gastric curvature by transverse colon, altering shape of stomach.

STOMACH.   Descensus of the stomach may be the result of
one or two factors: If the force acting on this organ is not from
below (colon, as is usually the case), the sagging is part of a
vicious circle which includes a ligamentous elongation involving the
attachments of the liver and spleen, and possibly the presence of
mobile kidneys.   The gastrohepatic omentum is never a robust

structure, but usually is thin, devoid of fat, and transparent. The lateral borders are thicker than the median portion.

Owing to its anatomical structure, this omentum is insufficient to act as an effective suspensory ligament of the stomach, since in addition to the stomach this structure must also maintain the superior position of the transverse colon, which usually lies closely
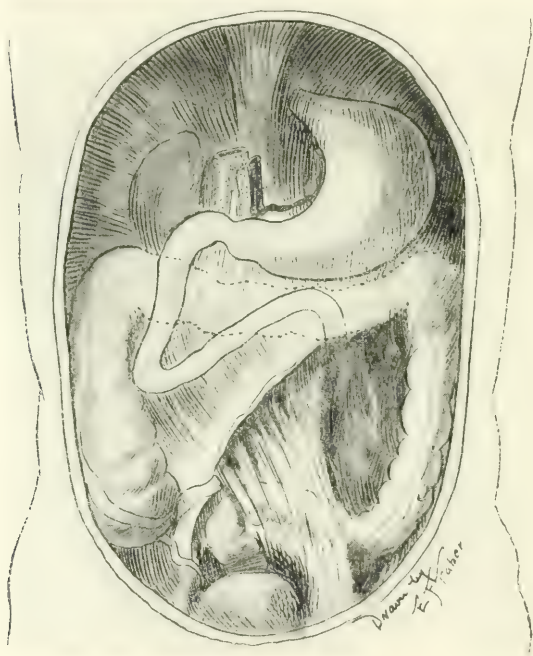
FIG. 4.—V-shaped duodenum lying to right of vertebral column.   Bands from under surface of mesentery to sigmoid colon.

related to the greater gastric curvature. While plication of the gastrohepatic omentum in some cases may support an empty stomach and colon, the additional weight of these hollow viscera, when filled with foreign material, is a factor of great importance.

The second and most important factor inducing a gastroptosis is the anatomical relationship of the transverse colon to the

stomach. While gastroptosis is almost always accompanied by
a descensus of the transverse colon, the reverse is not necessarily
the case, as will be shown later. The omental attachment of
the transverse colon to the greater curvature of the stomach is
firmer and much stronger than the attachment of the lesser gastric
curvature to the liver. It follows, therefore, that yielding on
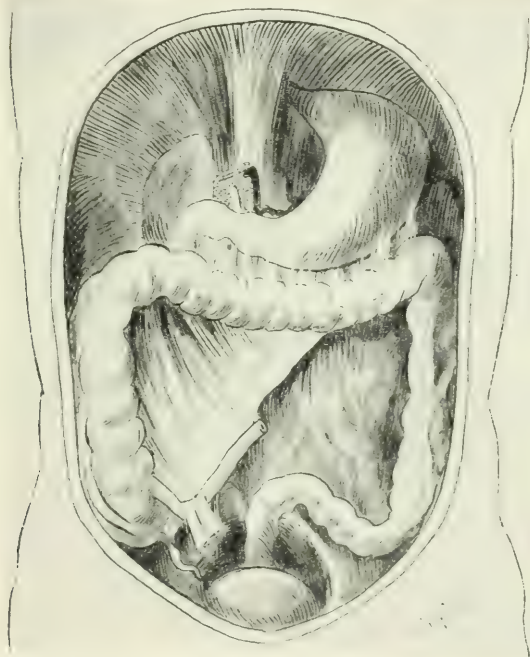
FIG. 5.—"Lane's kink of ileum." Note mesenteric band angulating terminal ileum and fixing
same to right sacro-iliac joint.

the part of the lesser omentum will be more frequently observed,
a deduction borne out by examinations both on the dead and the
living subject. Of all factors tending to produce gastroptosis,
therefore, the partial suspension of the transverse colon by the
stomach is the one which appears to account most logically for
ptosis of this organ. The descent of the stomach manifests itself
in a tendency to alter the shape and lumen of the duodenum, and

therefore symptoms ascribed to gastric are in reality of duodenal origin. The alterations in contour of the stomach are shown in Figs. 1, 3, and 9.

DUODENUM. Any departure from the normal in the anatomical arrangement or disposition of the small intestinal coils is dependent upon the development (length and attachments) and shape of the
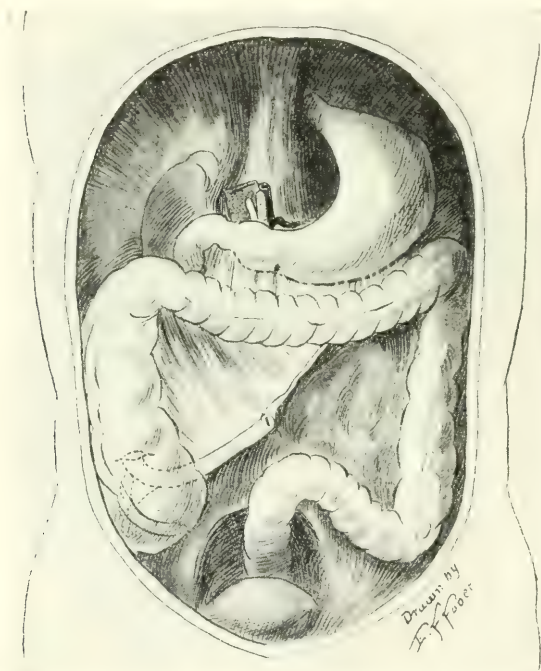
FIG. 6.—Ileocecal opening on dorsal cecal aspect. Terminal ileum lying behind cecum.

mesentery. Careful inspection has shown anomalous conditions either at the beginning of the small intestine (duodenum), or at its termination (Lane's kink of the ileum). Proper emptying of the stomach is dependent upon the free patency of the duodenum, which is determined by its course and muscular tone, as well as by the pyloric sphincter action of the stomach. Its patency is altered at once by compression or traction.

When the duodenum assumes a decided V-shape, the lumen is constricted so as to produce an acute angulation, which is sufficient to impair the proper drainage of this organ. The absence or presence of a well-defined ligament of Treitz is important in determining the acuity of the duodenojejunal flexure. An anatomical relationship of considerable importance is the relation
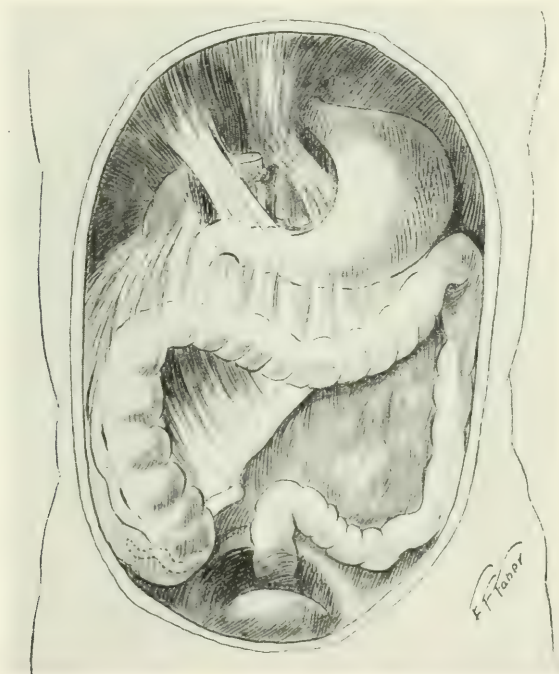
Fig. 7.—Cecal ptosis dragging down hepatic flexure. Note the great dilatation of the ptosed cecum and ascending colon.

of the superior mesenteric artery to the anterior surface of the third portion of the duodenum. This large artery passes over the duodenum, emerging from beneath the inferior surface of the pancreas. The weight of the coils of the small intestine, which hang suspended from this vessel embedded in the mesentery, is sufficient to induce a tension of the vessel which, acting on the

surface of the duodenum, will mechanically cut off the patency of its lumen. The practical importance of this observation has already attracted the attention of many surgeons, who assure themselves that no torsion of the mesentery exists in this region before closure of the abdominal incision.
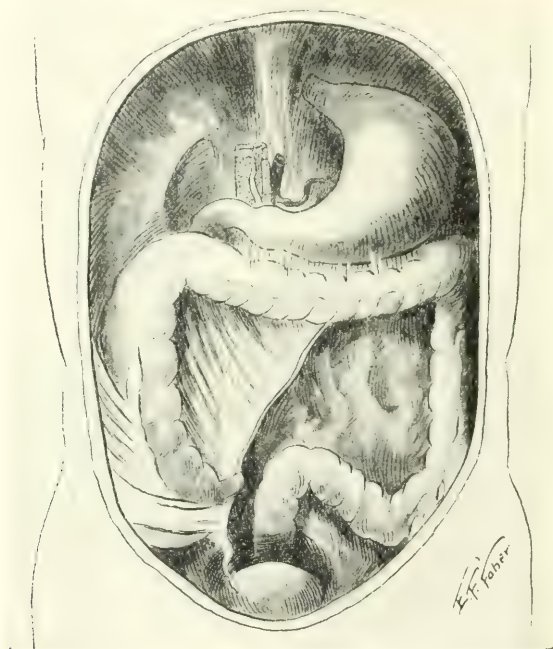
Fig. 8.—Peritoneal bands passing to anterior surface of cecum and ascending colon. These are peritoneal folds due to cecal ptosis.

The abrupt occurrence of postoperative gastric dilatation may be due to duodenal closure from this external force. Since the prone or knee-chest postures adopted in treating such patients are the attitudes most conducive to relieve this pressure on the anterior duodenal surface, the assumption that these anatomical factors underlie the production of this condition seems, at least partially, to be sustained by measures taken for relief.

The patency of the jejuno-ileum is conspicuously free of obstructive factors until we reach the terminal portion of the small bowel. Lane has well emphasized the acute angulation of the ileum in the vicinity of the ileocecal valve by the production of a stout band of tissue, which becomes separated from the mesentery and passes to the region of the right sacro-iliac joint. This
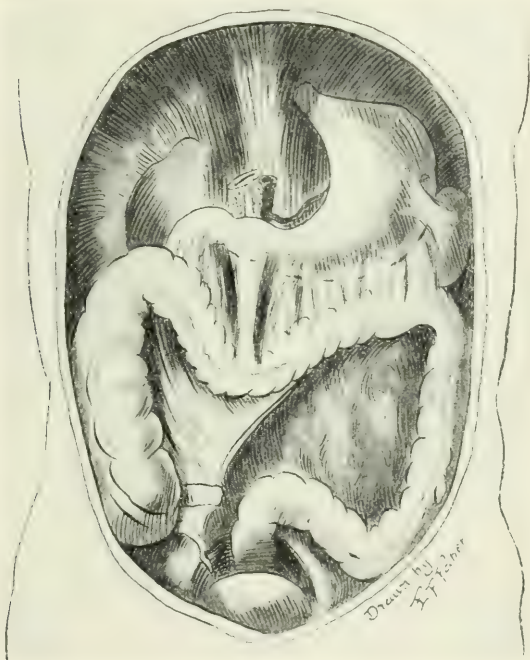
FIG. 9.—Dilated cecum and ascending colon owing to narrowing of lumen of colon at splenic flexure.

band is by no means a constant structure, and is not limited to the very end of the ileum. Similar bands are also sometimes seen tying the ileum to the right iliac fossa and involving the appendix. I would add to Lane's so-called "kink of the ileum" the immobility of the ileum often observed when the terminal portion of the small intestine is firmly bound down in the vicinity

of the right sacro-iliac joint. The latter condition is only a result
of an exaggeration of the forces which act to produce the first
variation.

It is obvious that this mechanical obstruction at the termina-
tion of the small bowel will offer much interference to its proper
drainage, as illustrated by the dilatation observed in the portion
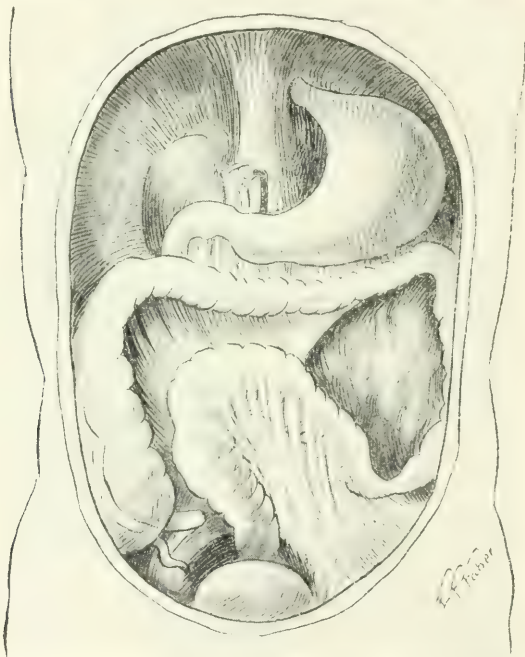
Fig. 10.—Immense cecum and ascending colon, and sigmoid colon, owing to strictures at
hepatic flexure and beginning of sigmoid colon.

of the small intestine proximal to the stricture. The kink is of
V-shape, with the apical point directed either above or below.

The causes for stasis of the small intestine are best sought in
this locality.

COLON. Cecal ptosis is quite common, and often exists to a
degree which causes this portion of the large intestine to hang

over the brim of the pelvis. The effort to compensate for this departure from the normal, on the part of nature, is the production of bands which pass from the lateral parietal peritoneum to the lateral and ventral surfaces of the cecum and ascending colon. Whether these bands represent the cause or the effect is a question open to discussion. The ascending and descending
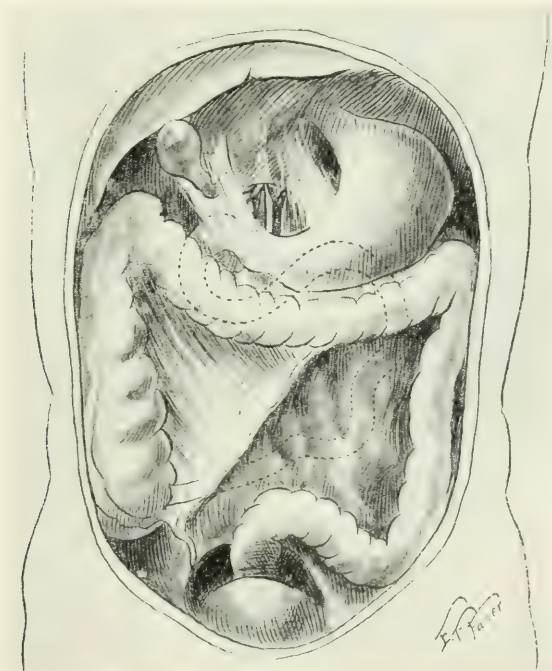
Fig. 11.—Marked hepaticoduodenal ligament. Sharp angulated hepatic and splenic flexures.

colon in 18 per cent. of cases (Jonnesco) has a mesentery. The absence of a mesentery in the case of the cecum is explained on the basis that this portion of the colon is never anchored in place, and is probably movable throughout life. Its original position is subhepatic, and from this position it grows down into the right iliac fossa. Should the adhesion of the lateral cecal wall to the parietal peritoneum take place, the primitive broad peritoneal

reflection becomes converted into one or more well-marked attenu-
ated bands, owing to the muscular contractions of the partially
fixed cecum in its efforts to disengorge itself. Reasoning in
this manner, the presence of these bands is not so much an
attempt on the part of nature to compensate for an anomalous
defect, as the direct result of faulty development, tending to ob-
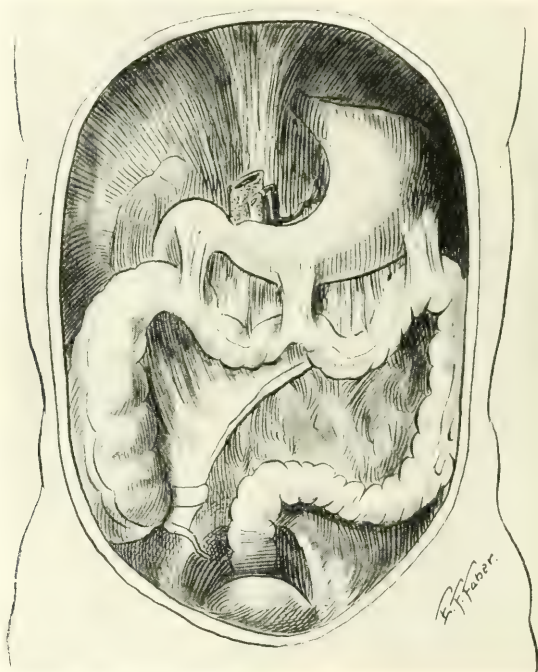
Fig. 12.—Peritoneal bands passing from greater gastric curvature to transverse colon.
Note suspension by stomach of transverse colon.

struct the physiological purpose of the cecum. These bands are
fairly common, and are not confined to the cecum and ascending
colon. I have seen such adhesion to the abdominal wall often
involving the summit of the sigmoid colon.

The ileocecal junction is one of considerable interest, and often
presents interesting variations. The kink in the ileum at its

termination, and the complete immobility frequently encountered, are two of the three anatomical factors involving this important break in the continuity of the gut tube. The other variation of considerable importance is the mode of insertion of the ileum into the cecum. The ileum not infrequently appears to lie behind the cecum and to project into the lumen from this peculiar position.
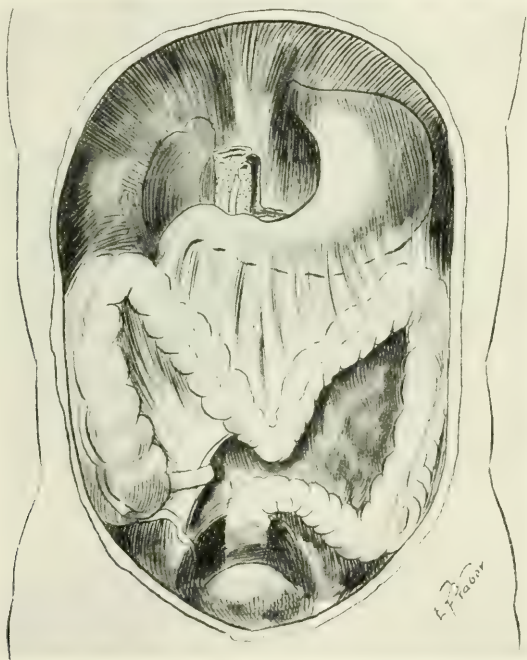
FIG. 13.—V-shaped ptosed transverse colon. No ptosis of stomach owing to long gastrocolic omentum. Note development of bands in gastrocolic omentum.

When filled, the entire weight of the cecum lies on the ileum at its junction and compresses the ileocecal aperture.

The mesentery of the appendix has long been known to be a factor of considerable importance in sustaining the position of the cecum in the iliac fossa. The appendix should properly co-operate in this manner, since the meso-appendix is derived from

the mesentery of the small intestine and is definitely fixed to the posterior wall of the body cavity.

Ptosis of the cecum exerts traction on the meso-appendix, with the subsequent interference with the patency of the lumen and the blood supply of the appendix.
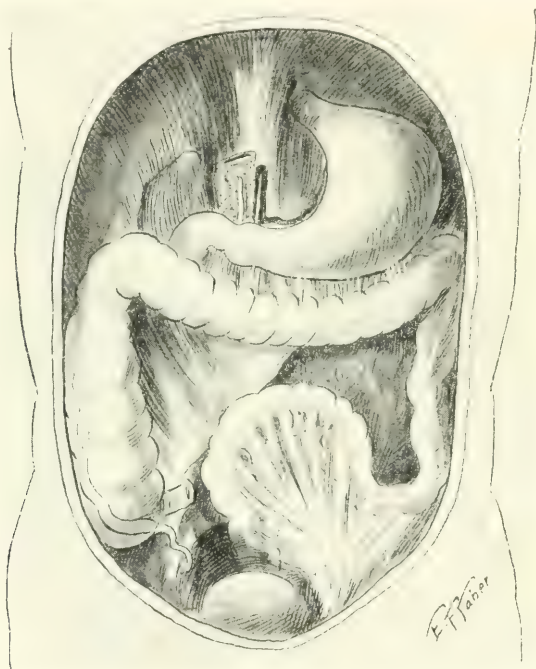
Fig. 14.—Large sigmoid with mesenteric bands on under surface. The sigmoid was adherent to the anterior abdominal wall.

Great cecal dilatation is almost invariably the result of acute angulation of the colon at one of the flexures. This resultant narrowing of the bowel lumen may be marked at the hepatic or splenic flexures, or the transverse colon may present one or more points of constriction produced by peritoneal bands.

This dilatation may be developed to an extraordinary degree without the ascending colon sharing in the process. The degree of acuity of the hepatic flexure is the result of two opposing forces:

(1) The colon may be anchored to the inferior surface of the right
hepatic lobe by peritoneal attachments of the liver, gall-bladder,
and duodenum. The adhesion to the gall-bladder and duodenum
is frequent and throws the support of the colon upon the hepatico-
duodenal ligament which represents the thickened right border
of the gastrohepatic omentum. (2) The marked fixation of this
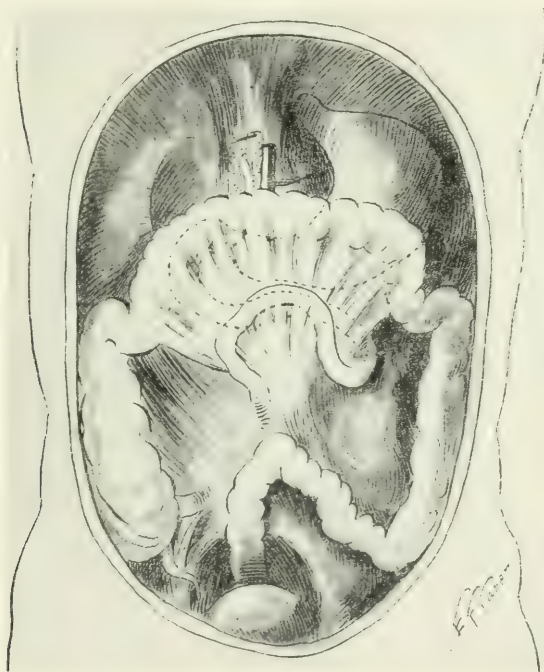
Fig. 15.—Adhesion of loop of small intestine to under surface of transverse mesocolon.

flexure with the subsequent dragging of a much distended trans-
verse colon is sufficient to narrow the lumen of the bowel in this
region to an extraordinary degree. If the colonic ptosis is com-
plicated by a gastroptosis, the superadded weight of the stomach
only tends to increase the forces at work, narrowing the lumen
of the bowel at this flexure.

The transverse colon may occupy a position high up in the

epigastrium, or describe a loop reaching as low as the crest of the pubes. This portion of the large bowel, both in the living and in the dead, more frequently lies on a level with the umbilicus than above this point. Extreme types of ptosis of the transverse colon accentuate the hepatic and splenic flexures, by rendering the sigmoid angulation at these turning points in the course of the bowel more acute. The stomach may follow the transverse
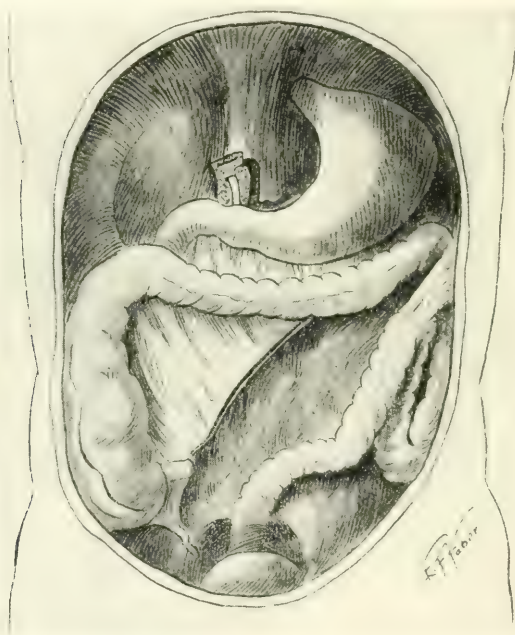
Fig. 16.—Anomalous sigmoid, producing a second splenic flexure of the colon.

colon in its downward course, although the gastric descensus is determined by the length of the transverse mesocolon, as well as by the length and strength of the gastrohepatic omentum. The descent of the transverse colon is not necessarily accompanied by descensus of the stomach, but the reverse is always the case, since the transverse colon and its mesentery are very important structures in the formation of the so-called stomach bed.

It would seem, therefore, anatomically impossible for gastroptosis of any degree to exist without an accompanying transverse colonic ptosis.

The transverse colon may present one or more abrupt breaks in the line of continuity, owing to sharp angulations produced by variations in the omental structure attaching this portion of the
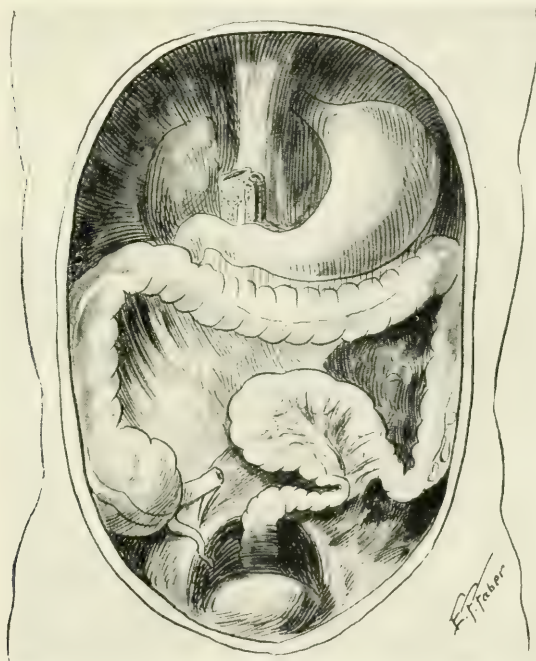
Fig. 17.—Cecal ptosis. Narrow basal attachment of sigmoid colon by stout mesentery, causing narrowing of the lumen of the proximal and distal portions of this bowel segment.

gut tube to the body wall. Bands passing upward over the anterior facies of the stomach, or downward to become continuous with the mesentery of the small bowel, are frequently observed.

What is true of the hepatic flexure obtains in the consideration of the splenic angle of the colon. One often sees enormous dilatation of the cecum, ascending and transverse colon, abruptly terminating at the splenic flexure. The reason is at once apparent,

since examination of this region discloses a sharp sigmoid curve with narrowing of the lumen of the bowel at this point. Below this flexure a narrow and contracted descending colon is usually observed. So constant is this observation that first inspection of the viscera, when the abdomen is opened, will disclose the individual dilated segments of the colon, and the distinct limitation of the distention of the gut will localize the obstructing factor at the distal end of the enlarged loop.

The descending colon is probably subject to less anatomical variation than any other portion of the large bowel. The downward course of the fecal current, in the absence of obstruction of the bowel lumen at the sigmoid colon, is designed to cause the least possible trouble in the discharge of the bowel contents.

The sigmoid loop of the colon is subject to variation to a degree sufficient to preclude a statement of what constitutes a normal sigmoid. Several factors are of noteworthy importance in considering anomalous conditions of this portion of the gut tube.

1. The sigmoid may be tightly tied down at its beginning by a short thick mesentery which constricts the lumen of the bowel when it describes the curve which is obliquely forward and to the right.

2. This loop of the large bowel may describe three-fourths of a circle, and the completion of the ring is occupied by the narrow basal attachment of the mesentery. A constriction of the gut in this region produces an enormous distention and a thinning of the intestinal wall. The musculature of the bowel obviously suffers in consequence and the expelling force is proportionately decreased.

3. One observes variations in the length of the sigmoid from 12 to 28 inches, and the tendency to compensate for the overmobility and angulation of the bowel at this point is the production of tense bands in the mesosigmoid, some of which are almost of tendinous consistency.

4. The sigmoid may be no larger than the small bowel at its widest part. This is observed in those examples of a rather short sigmoid which passes over the promontory of the sacrum to the right sacro-iliac joint, and descends obliquely downward to termi-

nate in the rectum. The bowel is tightly held to the structures over which it passes, is not mobile, and mesenteric bands pass to the under surface of the mesentery of the small intestine. The lumen of the sigmoid of this type may show one or more marked constrictions. This is an anomaly of developmental origin, since the original common mesentery of the early undifferentiated gut tube became attached to the posterior body wall in a faulty manner, with failure of separation of the mesenteries of the small and large bowel.

5. Enormous dilatation and elongation of the sigmoid are compensated for on the part of nature by the production of adhesions to the ventral peritoneal surface of the body wall. These are true adhesions, probably pathological in nature, and are not due to faulty development.

WHAT CASES OF CONSTIPATION ARE AMENABLE TO SURGICAL TREATMENT?[1]

By JOHN G. CLARK, M.D.

FROM the observations of my associates, Dr. Floyd Keene and Dr. Ginsburg, on the embryological and anatomical defects occurring in the gastro-intestinal tract, taken in conjunction with our clinical cases, it is quite evident that many of the supposed cases of functional constipation have a long existent anatomical etiology.

As we have analyzed the types of constipation, we find that relief by surgical means is largely applicable to this particular class. It is farthest from our intention to hold out the view that the neurasthenic individual of constipated habit can be relieved by surgical measures. One, therefore, must carefully differentiate between what might be classed as a functional and a pathologically anatomical constipation.

This differentiation is not always easy. A clinical rule which I have established for guidance is to ascertain, first, the duration of the constipation, as to whether congenital or acquired; and secondly, as to the means necessary to effect an evacuation of the bowel. Thus, one patient will give a history that she suffers greatly with constipation, and yet one discovers that a small dose of cascara is quite sufficient to regulate this function. Any suggestion of surgical intervention in such a case would, of course, be the height of absurdity. Even in those cases in which a larger dose of purgative medicine is required, especially if the general health of the individual is good, one would not consider surgical measures.

[1] Read March 1, 1911.

The summary of the entire question, therefore, hangs upon whether there is a definite anatomical defect constituting a partial obstruction. In such cases the patient may go days, even after the use of more or less drastic purgatives, without a satisfactory clearing of the lower bowel. At the same time there is more or less tympanites and distress either in the cecal or sigmoidal areas, or at the colonic flexures.

In the order of topographical observation of colonic defects we have noted the colicky pains incident to a descensus of the cecum, which, instead of resting at the brim of the pelvis, drops as a dilated pouch into the cul-de-sac. Quite recently Wilms has called especial attention to this defect, and finds that in several cases in which there was persistence of symptoms after the removal of a supposed offending appendix a subsequent operation for the elevation and fixation of the cecum in its normal situation relieved the symptoms. He ascribes the colicky pains in this area to the failure of peristalsis and antiperistalsis to carry the food content upward, and finally past the hepatic flexure into the transverse colon.

According to our viewpoint, however, we are more inclined to ascribe these symptoms to a defective emptying of the ileum into the cecum. It is a reasonable view that a cecum overloaded with semipultaceous matter which remains as a stagnant mass in the cecum must retard the flow of liquid food from the ileum into the cecum, and consequently cramp-like pains at the ileocecal region occur as a result of limitation of the peristaltic wave. The trouble is noted about the flexures more particularly when there is either a marked ptosis of the transverse colon, or an actual dislocation of the flexures, giving rise to an irregular crumpling of the colon in the lower part of the abdomen. Marked redundancy of the sigmoid flexures also, especially when there have been years of progressive constipation, may give rise to symptoms varying from exaggerated constipation to actual obstruction. Fortunately a strangulation is but seldom noted. Indeed, it is astonishing, when one sees the marked variations in length which take place in the sigmoid flexure, that serious obstructions do not occur more frequently.

When we first began to apply the x-rays to these cases for diagnostic purposes, we were inclined to view many cases as being seriously anomalous which we have since considered approximately normal. Treves many years ago pointed out the fact that one-fourth of all autopsies showed the loop of the transverse colon dependent in the pelvis, and he interpreted this as a significant possibility in the production of excessive degrees of constipation. As a result of our clinical experience, however, we view these cases only from the standpoint of the functional coefficient of the colon, for every surgeon has noted even exaggerated degrees of colonic ptosis without any marked degree of constipation.

It is not possible, therefore, to establish an anatomical rule for the treatment of these cases, and as I have repeatedly stated, it is not for the surgeon to initiate the treatment, for the patient should have careful medical supervision first, to determine whether the colonic function can be properly adjusted by medical means. Only on medical failure can we justifiably accept these as surgical cases, and even then we must be guarded in our promises of relief. In my service at the University Hospital we have operated upon over 50 of these cases. Of this number, we can claim 48 per cent. of cures. Of the remainder, some are improved, others are no better. These, however, represent the exaggerated types, many of which could only be left to drag out a more or less wretched existence, relying solely upon drastic purgation and copious enemata to empty the colon.

We have not yet reached the point when we can accept with enthusiasm Lane's principle of radical extirpation of the colon with anastomosis of the ileum into the sigmoid. However, I am sure that in the exaggerated cases, where there is great redundancy and dilatation of the colon, occasionally this measure may be the only one that can possibly be instituted with any hope of relief. One cannot, however, be too careful in advising operations in such classes of cases, for we have all witnessed the operative mania which has been instituted in cases of movable kidney, and even the very beneficial operation of gastro-enterostomy has been

grossly misapplied in the hands of the operative novice or enthu-
siast, who wields the scalpel with greater facility than he exercises
his judgment.

These cases may be studied carefully so that those which are
amenable to treatment by surgery may receive benefit, and avoid
that large number in which surgical measures are of no value.
Operation in this large class may constitute, because of their
failure of relief, a bar to the investigation of those cases in which
mechanical principles alone can be invoked for their relief.

In conclusion, therefore, one may state that all cases of consti-
pation should have the care of a physician, and only after his
failure should surgical measures be considered, and then only when
the symptoms are of a more or less obstinate nature. If this rule
is followed, a very definite percentage of satisfactory results will
be obtained in the operative treatment.

As definite conclusions cannot be reached concerning the
results of this or any other operation until at least a year has
passed, we have excluded all cases that have been operated upon
during the last year. The results of those from which we have
been able to secure accurate information are as follows:

Suspension of sigmoid flexure, 5 cases—3 cured, 2 unimproved.

Suspension of transverse colon (ventro-omental fixation), 6
cases—2 cured, 3 improved, 1 failure.

Excision of sigmoid, 3 cases—1 cured, 2 improved.

Excision of sigmoid and suspension of transverse colon, 1 case—
cured.

Lateral anastomosis from one limb of sigmoid to the other, 2
cases—1 cured, 1 died a year later from some unknown illness.
Her physician reported marked improvement after her operation.

Excision of transverse colon, 3 cases—1 almost entirely well, 1
improved, 1 unimproved.

Three fatalities have occurred—1 death from peritonitis, 2
from acute gastric dilatation.

As a summary of my views upon this subject, expressed in the
Chairman's Address before the section on Obstetrics and Diseases
of Women, at St. Louis, I may offer the following:

1. Developmental anomalies are at the bottom of many cases of chronic constipation.

2. Defective posture of the body is frequently a result rather than a cause of this ptosis.

3. Congenital potential factors are present in many individuals which become active through accident, such as traumatism, rapid and badly cared for childbirth, habitual constipation, operative adhesions, etc.

4. Neurasthenia often dates from childhood or puberty; operation, therefore, in the adult may give only partial relief because of this constitutional asthenia.

5. Cases in which there is a recent acquirement of the active factor give the best surgical results.

6. Various suspension operations are valuable in properly selected cases, but disappointing in the remainder. At best these fixation points may be unstable.

7. Radical excision of obstructive portions of the large bowel may give the highest percentage of operative mortality, but it is likely to give the best ultimate results in the survivors.

8. In no field of surgery should haste be made slower than in this. It is not a field for the novice.

9. The most important factor in the diagnosis is a detailed clinical history pointing accurately to obstructive possibilities. A well-taken skiagraph is of the greatest confirmatory value.

DISCUSSION.

Dr. John H. Gibbon: The question of anomalies of the colon and what can be done for them surgically is a comparatively new and very interesting one, but one about which I do not believe we are able at the present time to reach absolutely definite conclusions. After seeing the picture shown by Dr. Keene and Dr. Ginsburg, it is probably impossible for us to say exactly what is the normal colon. Regarding the choice of cases to be operated on, I can subscribe to all that Dr. Clark has said. The colon may appear to be very anomalous and yet be capable of per-

forming its function. If it does not perform its function, very definite indications of it arise, such as chronic obstruction of the bowels. When a colon, which has been chronically obstructed, is exposed we will find both dilatation and hypertrophy, and unless these evidences are present at operation the mere presence of the colon in an apparently normal position does not indicate a pathological state. The cases to be operated upon are the ones that give rise to definite symptoms. I am referring, of course, to the operations of resection of the colon and of anastomosis for the purpose of side-tracking the colon. Mr. Lane, who has been the great advocate of operation in these cases, has, in my opinion, gone too far in recommending and performing these two types of operation. He believes that cystic degeneration of the breast may be caused by intestinal stasis, and he actually performs resections of the colon or side-tracking operations for the cure of hip-joint disease in young children. In regard to these operations, I think the occasional operator, or the enthusiastic young surgeon, needs to be careful in the selection of cases for operation. Dr. Clark has already said this, but there has been so much literature on this subject and so many conditions have been described as being anomalous and productive of disease, that a repetition of the warning is not amiss. It took the surgeon some years to learn what cases of movable kidney required operation, and many cases were operated upon that did not require it. No conscientious surgeon today operates upon a kidney simply because it is movable or because the patient presents a long line of neurasthenic symptoms. We now know the type of movable kidney that requires operation, we operate upon them, and we get good results. I would say that surgery of the colon was in the developmental stage, and that the radical operations under consideration should be left in the hands of the experienced surgeon. Of course, no one could question the advisability of operating upon a twisted sigmoid, but such a condition always gives rise to definite symptoms which plainly indicate the necessity for operation. For some time to come our difficulty will be not the performing of these operations, but in the choice of cases to be operated upon.

Dr. S. Solis Cohen: I should like to ask whether in this interesting study there has been found any large proportion of cases with narrowing of the lumen of the large intestine for a considerable distance. Occasionally in autopsies upon cases of pulmonary tuberculosis I have observed such narrowing of the whole of the colon. Recently, in a number of patients not tuberculous, studied by skiagrams taken at such intervals after the giving of bismuth that the whole course of the bismuth throughout the intestine could be traced, I have observed, along with angulations or misplacements or anomalies, whether of pathological degree or otherwise, considerable tracts of apparent narrowing with delayed emptying.

The possibility and propriety of remedying the chronic obstruction or chronic pain in such cases by resection of the narrow portions appears to be worthy of consideration. In some of these instances abdominal sections had been done, and the question of adhesions, of course, arises; but in others there had been no operative interference.

DR. GEORGE E. PRICE: Neurologists have found that neurasthenia is more apt to be the cause of gastro-intestinal symptoms than the result of disorders of the digestive tract. The study of congenital anomalies of the gastro-intestinal tract should prove of interest in such conditions as epilepsy, where gastro-intestinal auto-intoxication was a factor of importance; also in the degenerative psychoses. So far as I can recall, no such studies have been made.

DR. JOSEPH SAILER: I think we make a mistake in confusing neurasthenia with malnutrition. Many are not neurasthenic in the popular use of the term, but undernourished. Very often improvement in nutrition will bring about an anatomical correction of the part.

Dr. Gibbon said that it took the surgeons a long time to find out that movable kidney was not the cause of neurasthenia. I have only to remind him that this was not for lack of telling. If he will go back to the very able paper of Shiller, published in the early nineties, I think he will find the whole subject carefully discussed, and the results of surgical operation are criticised much by surgeons at the present day.

DR. JOHN B. SHOBER: I would like to take this opportunity of referring to a paper I had the honor of reading before this College in 1898, upon "Anomalous Positions of the Colon, with the Report of a Case Discovered at Exploratory Operation." This was long before the use of the x-rays in these conditions, and we were then unable to obtain such beautiful pictures as were represented on the screen this evening. At that time I had looked up the literature and reported some fifty cases of anomalous positions of the colon, embracing all the types represented here this evening. Of course, they had to be presented by word of mouth and by drawings. The conclusions reached at that time regarding these conditions were much the same as have been arrived at tonight. One point in the conclusions then reached, and not mentioned this evening, was in regard to the etiology. Many of these malpositions were considered to be the result of peritonitis occurring in fetal life, forming adhesions which would interfere with normal development and result in all kinds of deformities.

DR. JOHN B. DEAVER: I do not believe that postoperative dilatation of the stomach is due to any anatomical arrangement of the bloodvessels, etc.; I believe it due to infection or toxemia.

DR. ADDINELL HEWSON: One of the speakers stated that it was impossible to obtain the ages of the bodies investigated. If the gentle-

man will give me the number attached to the body I will give him the age as furnished me by the certificates.

I should like the gentlemen of the College of Physicians to know that the Anatomical Board of the State of Pennsylvania is at all times and upon every occasion willing to advance and to assist any and all scientific investigation.

DR. KEENE, closes: In answer to Dr. Price I would say that an article appeared during the last year in the *Journal of the American Medical Association* dealing with the possible relation between redundant sigmoid and epilepsy.

I wish to apologize, through Dr. Hewson, to the Pennsylvania Anatomical Board. At the beginning of my work I made inquiries concerning the possibility of obtaining the ages of these babies, and was told that such was impossible. It is quite evident that I was at fault in not seeking this information from the proper source.

DR. GINSBURG, closes: Dr. Cohen asked whether there was an unusual amount of narrowing of the entire lumen of the large intestine. We have observed it in a good many instances in which the large intestine was small from cecum to rectum, and look upon this condition as one which closely approaches a normal arrangement.

I did not mean to convey the impression that I was laying down a dictum which will explain the cause of acute dilatation of the stomach.

Many recoveries have been reported in this country and abroad, when patients with this condition were placed in the prone position. In some instances the knee-chest posture was tried, and recovery ensued. This form of postural treatment will, anatomically at least, relieve any ventral duodenal pressure, and hence the deduction of the cause of this condition being anatomical in nature.

THE ANATOMICAL EXPLANATION OF THE PARALYSIS OF THE LEFT RECURRENT LARYNGEAL NERVE FOUND IN CERTAIN CASES OF MITRAL STENOSIS.[1]

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During the last thirteen years there have been reported 37 cases of mitral stenosis with associated interference with or abolition of the movements of the left vocal cord. Study of the notes of those cases which came to autopsy shows so much variation in the structures which are described as causing pressure on the left recurrent laryngeal nerve that the present study was undertaken with the idea of attempting to clear up the discrepancies. Our work has consisted of an analysis of all the cases reported up to the present time, and of a careful examination of sections and dissections of hardened thoraces. Observations made in soft bodies are of questionable value, because the opening of the chest allows of so much collapse and the manipulations of dissection cause such a degree of distortion that normal relations are altered to a most astonishing degree. We therefore used only cadavers with everything hardened *in situ* by means of an arterial injection of formaldehyde solution,

[1] Read March 1, 1911.

in the endeavor to keep the thoracic and especially the mediastinal viscera as nearly as possible as they are *in vivo*.

HISTORICAL. The association of paralysis of the left recurrent laryngeal nerve with mitral stenosis was first described by Ortner, in 1897, as occurring in two cases which had come under his observation. He ascribed the paralysis to compression of the nerve between the arch of the aorta and the distended left auricle. The nerve in his cases was discolored, compressed, and ribbon-like. In the following year Herrick recorded a case in which, in addition to a dilated left auricle, chronic adhesive pericarditis was found, the nerve being embedded in a mass of cicatricial tissue as well as compressed by the auricle.

In 1901 Kraus reported a case of left recurrent paralysis associated with mitral stenosis. He took exception to the anatomy of Ortner's explanation, and described the mechanism in his case quite differently, taking the ground that the laryngeal paralysis, although associated with marked left auricular dilatation, was indirectly due to hypertrophy of the right ventricle. This condition, by altering the position of the heart as it lay on the diaphragm, was assumed to alter the relationship between the pulmonary artery, the aortic arch, and the aortic ligament in such a way as to cause the ligament to drag upon the recurrent laryngeal nerve. In his case the aortic ligament is stated to have run more horizontally than is normal, so that the left recurrent laryngeal nerve did not course laterally from the aortic ligament around the aortic arch, but crossed the latter. At the point at which the nerve crossed the aortic ligament it was constricted and discolored.

In v. Schroetter's case the nerve is reported as having been compressed between a patulous ductus arteriosus and the aortic arch, and in Frischauer's case, between the left pulmonary artery and the aorta, the former being pushed upward by the dilated left auricle. Hofbauer described the compression as occurring between the dilated pulmonary artery and the aorta, while in Bonardi's and in two of Osler's cases we are again told that the left auricle impinged directly upon the aorta. In Osler's third case there was no autopsy.

In Gantz's case the nerve is stated to have been pressed upon by enlarged peribronchial and peritracheal glands. Despite the co-existence of a severe pneumonia and pleuritis, he attributes this glandular enlargement to stasis produced by a weak heart. No similar explanation is to be found in the literature of the subject. In Mead's case the compression was presumably exerted by the greatly dilated pulmonary artery, although a patulous ductus arteriosus was also found.

Little of clinical interest is reported concerning the laryngeal symptoms, although in some of the cases it was noted that the hoarseness was more marked in certain positions. Thus, Hofbauer's patient was less hoarse in the dorsal and right lateral postures, while Prota's[1] was more hoarse when the head was rotated to the left.

The paralysis may apparently be bilateral. In seven of Quadrone's eight cases both cords were paretic. In explanation of this he assumes that the brachiocephalic and subclavian arteries may sustain the brunt of the cardiac displacement. It is on this basis that the inequality of the radial pulses sometimes met with in cases of mitral disease has been explained (pressure of the auricle upon the aortic origin of the left subclavian artery). Thus, Massei[2] and Perotta hold that right-sided recurrent paralysis in mitral stenosis is never found as an isolated or primary lesion, but only as an exaggeration of those conditions which brought about the left recurrent paralysis. As a matter of fact, the entire situation, especially when the right recurrent is concerned, is so clouded that it is eminently desirable that future autopsies should be made with greater care, or, as Kraus has suggested, not made as routine autopsies, but as frozen sections. None of the cases in which the right nerve was implicated have come to autopsy.

Anatomic Considerations. The left recurrent nerve springs from the vagus as the latter is passing down the sinistro-anterior aspect of the horizontal part of the aortic arch (Fig. 1). It hugs the aorta closely and passes under the arch either at the point at

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[1] Su due casi di emiplegia laryngea con singulare disturbo disfonico. Atti del Terzo Congresso d. Soc. Italiana di Larengologia, 1899, p. 230. (No pathological findings in thorax in either case clinically. No autopsies.)

[2] Quoted, Boinet, loc. cit.

which the ligamentum arteriosum joins the latter vessel or slightly anterior to this position (Fig. 1). Reaching the dextro-posterior

Fig. 1.—Sagittal section 3 cm. to the left of the midsternal line, viewed from the left: *A*, left subclavian artery; *B*, retracted pleura; *C*, left vagus nerve; *D*, arch of aorta; *E*, left recurrent laryngeal nerve; *F*, ligamentum arteriosum; *G*, left superior pulmonary vein; *H*, pulmonary aorta; *I*, reflected pericardium; *J*, right ventricle; *K*, moderator band; *L*, right ventricle; *M*, apical mediastinal pleura; *N*, *P*, retracted upper lobe of left lung; *O*, left pulmonary artery; *Q*, left bronchus; *R*, left inferior pulmonary vein; *S*, left auricle; *T*, mitral leaflet; *U*, left ventricle; *V*, cut surface of left lower lobe.

side of the arch, it ascends, its further course having no bearing on the clinical condition under discussion.

The bifurcation of the pulmonary aorta takes place at the lower inner margin of the left bronchus, about 2.5 cm. from the bifurcation of the trachea. The angle lies behind the left margin of the

Fig. 2.—View of a dissection of the posterior mediastinum from behind: *A*, left subclavian artery; *B*, left recurrent laryngeal nerve; *C*, aorta; *D*, left pulmonary artery; *E*, left superior pulmonary vein; *F*, left inferior pulmonary vein; *G*, left ventricle; *H*, aorta (reflected); *I*, left bronchus (reflected); *J*, right bronchus (reflected); *K*, cut end of esophagus; *L*, superior vena cava; *M*, descending part of aortic arch; *N*, ligamentum arteriosum; *O*, angle of bifurcation of pulmonary aorta; *P*, right pulmonary artery; *Q*, left auricle; *R*, right superior pulmonary vein; *S*, right middle pulmonary vein; *T*, right inferior pulmonary vein; *U*, inferior vena cava; *V*, esophagus (reflected).

ascending part of the aortic arch and above and in front of the root
of the left upper pulmonary vein (Figs. 2 and 3).   The right branch
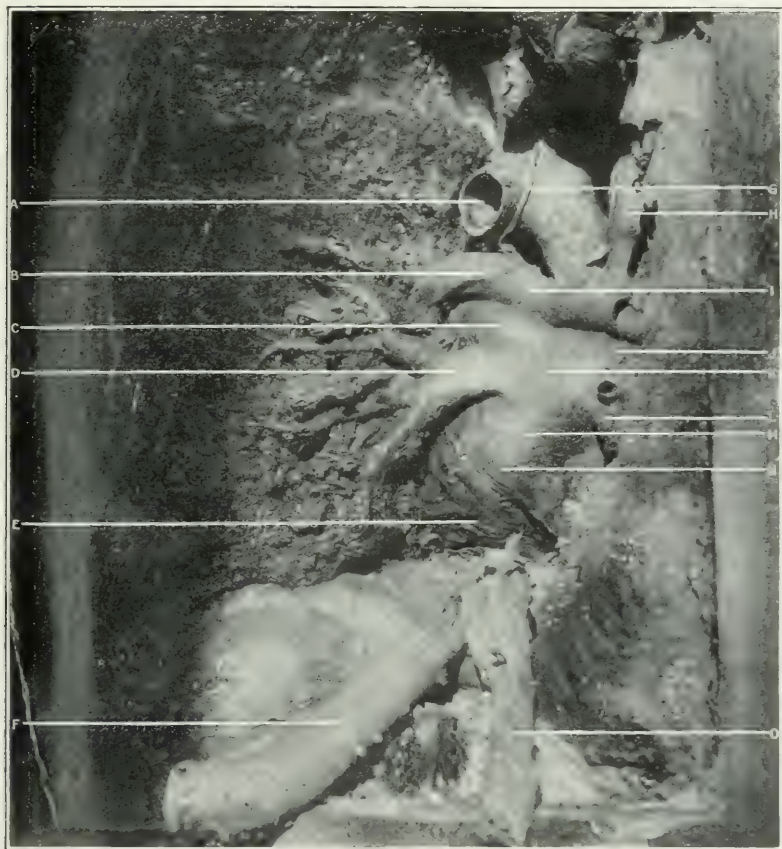
FIG. 3.—Oblique view from the right of a dissection of the mediastinal viscera from behind:
A, aorta; B, left pulmonary artery; C, left superior pulmonary vein; D, left inferior pul-
monary vein; E, left ventricle; F, thoracic aorta (reflected); G, left recurrent laryngeal
nerve; H, superior vena cava; I, angle of bifurcation of pulmonary aorta; J, root of right
superior pulmonary vein; K, M, left auricle; L, right inferior pulmonary vein; N, coronary
sinus; O, esophagus (reflected).

passes horizontally to the right under the aortic arch and above
the left auricle. It does not enter the present problem. The left
branch curves over the left superior pulmonary vein and the left

bronchus, both of which it indents, and passes outward and markedly backward, forming an angle with the right branch of about 100 degrees in the horizontal plane. Above, and 4 mm. away from it, is the beginning of the descending part of the aortic arch, to which it is connected by the ligamentum arteriosum (Fig. 1). The descending part of the arch continues down in contact with the posterior mesial surface of the left pulmonary artery. Below the left pulmonary artery lie the left superior pulmonary vein and the left bronchus (Figs. 2 and 3).

The appendix of the left auricle is curled around the root of the pulmonary aorta. It projects upward in the angle between the left pulmonary artery and the left superior pulmonary vein (Fig. 4).

The ligamentum arteriosum (the obliterated ductus arteriosus) is a fibrous cord, about 3 mm. thick and 2 cm. long. We have found that it lies almost exactly in the anteroposterior plane of the body and ascends but slightly as it passes backward from the left pulmonary artery to the aorta (Fig. 1). In or slightly anterior to the obtuse angle formed at its junction with the latter vessel lies the recurrent laryngeal nerve.

In effecting pressure on the nerve there are two conditions at work —increase in size and alteration of position, both dependent upon the narrowing of the mitral orifice. Changes in size, viz., enlargement, involve in sequence the left auricle and appendix, the pulmonary veins, and the pulmonary arteries. The obstruction to the blood current in the mitral orifice results, first, in a dilatation of the left auricle and its auricular appendix. Rise of pressure in this chamber is followed by the same condition in the pulmonary veins, which results in their overfilling and distention. This in time dams back the blood in the lungs and tends to cause its stagnation in the pulmonary artery and in the right heart. In consequence there is always present a dilatation of the left auricle and of the pulmonary arteries and veins, which gives rise to a crowding of the mediastinal structures at the base of the heart.

Changes in position are mainly due to the distention of the auricle, although this can be aided materially by enlargement of the right heart, particularly of the ventricle. Some remarkable instances of

left auricular dilatation have been recorded. According to Witwicki,[1] the left auricle is the most distensible of all the heart chambers, and Samuelson[2] has stated that occlusion of the left coronary artery causes a flaccid dilatation of the auricular walls, which may assume the appearance of a distended bladder. Minkowski[3] re-
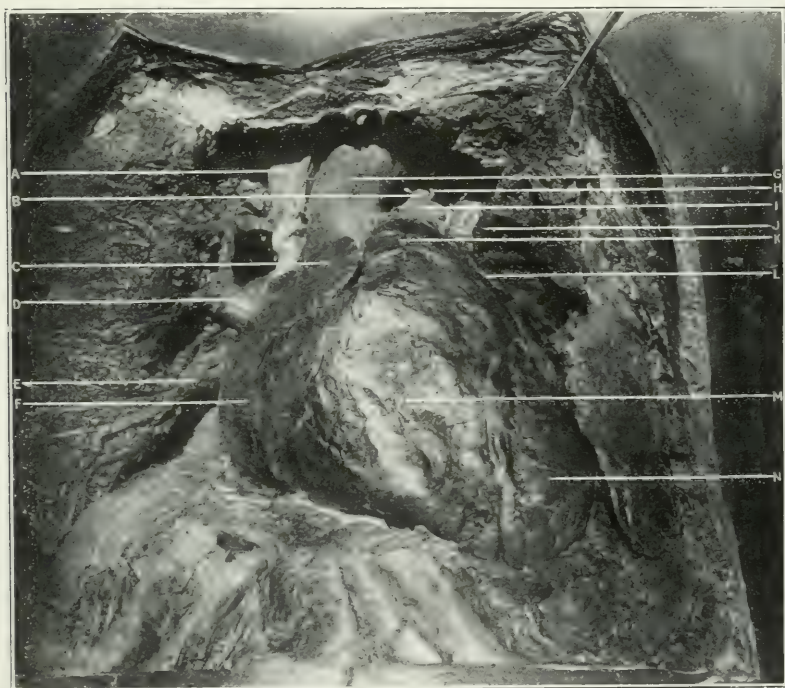
FIG. 4.—View of a dissection of the mediastinal viscera from in front: *A*, anterior vena cava; *B*, ligamentum arteriosum; *C*, right auricular appendix; *D*, right superior pulmonary vein; *E*, right inferior pulmonary vein; *F*, right auricle; *G*, arch of aorta; *H*, left recurrent laryngeal nerve; *I*, left pulmonary artery; *J*, left superior pulmonary vein; *K*, pulmonary aorta; *L*, left auricular appendix; *M*, right ventricle; *N*, left ventricle.

moved a heart at autopsy which contained about 4 liters of blood, of which nearly 3 were found in the left auricle. This specimen was obtained from the body of a man, aged thirty-two years, who had suffered from double mitral and tricuspid lesions and in whom a diag-

[1] Zeit f. klin. Med., 1895, xxvii, 321.   [2] Soc. Anat., Paris, vol. ii.
[3] Münch. med. Woch., 1904, p. 182.

nosis of mitral stenosis had been made fourteen years before his death. Despite this enormous dilatation the patient had been able to walk about until but shortly before his demise. The auricular walls were thin and membranous. In the case reported by Briquet[1] the left auricular capacity was 650 c.c. (the normal average being 55 c.c.), or what is practically equal to the capacity of a whole normal heart. Müller[2] has recorded an instance in which the left auricle was larger than a child's head, this occurring in a case in which the heart weighed 620 grams, the patient weighing only 65 kilograms. (Under normal circumstances a patient of this weight should have a heart weighing about 300 grams.) Toledano[3] reported a case in which the auricle measured 12 by 11 cm. Sansom has described the auricular wall as being attenuated to the thinness of a visiting card. Owen and Fenton[4] have reported a left auricle with a capacity of 900 c.c., a distention so great that aspiration was performed in the belief that a pericardial effusion was present.

It is well known that dilatation of the pulmonary artery is often encountered in long-standing cases of mitral stenosis, and not infrequently the artery undergoes considerable arteriosclerotic change. In these cases there is an area of dulness at the upper left margin of the sternum, sometimes sensitive to pressure or percussion, as well as enlargement of the right heart. Dmitrenko, in his case of pressure paralysis, succeeded in making graphic records of the pulmonary pulsation.

The left auricular cavity can expand readily in but one direction, viz., upward (Figs. 2 and 3); posteriorly, it rests against the aorta and esophagus; anteriorly, it is limited by the right auricle and the left ventricle, and below by the right auricle and the liver. In expansion, the auricular appendix would probably be the first part affected, as it lies free and unadherent to anything. Should it become dilated it would press upward and backward, thrusting the left pulmonary artery against the aorta, the left upper pulmonary vein against the left pulmonary artery, and forcing the distal portion

[1] De l'état du cœur gauche dans les lésions mitrales, Thèse de Paris, 1890.

[2] Zeit. f. klin. Med., 1905, lvi, 520.

[3] Soc. Anat., Paris, 1875.   [4] Clinical Society London, May 24, 1901.

of the latter against the aorta. Later, when the atrium or main cavity of the auricle dilates, the proximal part of the left pulmonary artery is jammed upward and backward, mainly by the root of the left upper pulmonary vein. The nerve is thus squeezed between the artery on the one hand and the aortic arch or the ligamentum arteriosum on the other. Frischauer and Hofbauer are the only ones who report finding this post mortem.

COMMENT ON PREVIOUS EXPLANATIONS. The foregoing facts should make us extremely cautious in accepting the reports of non-autopsied cases as examples of recurrent paralysis due to auricular pressure in the course of mitral stenosis. It should be borne in mind that the first examples of this condition were first reported fully thirty-five years after paralysis of the recurrent laryngeal nerve had first been described by Türck and Gerhardt (1862). Furthermore, the details of the cases reported by Koellreuter, in which the paralysis was in all probability due to a mediastinal neoplasm, and by Gantz and ourselves, in which glandular enlargement was the etiological factor, clearly show how closely the picture produced by mitral stenosis may be simulated by other causes and conditions.

The junior author has for the last six years been especially on the lookout for this conjunction of pathological conditions, and among many hundreds of cardiac patients seen during this time has met with only one case in which recurrent paralysis appeared to be due to mitral disease. There was, however, no autopsy, and the few notes which were made have been lost.

How easily one might be led into attributing left recurrent laryngeal paralysis to mitral stenosis is also illustrated in the following case, which occurred in the service of Dr. F. H. Klaer, in which a diagnosis of mitral stenosis was readily made and in which aortic aneurysm was suspected but later abandoned as the result of the x-ray examination, which disclosed the presence of enlarged bronchial lymph nodes.

W. A. H., male, aged twenty-nine years, a clerk by occupation, presented himself at the medical dispensary of the University Hospital on account of loss of weight (18 pounds), indigestion, and hoarseness when in the prone position. This latter symptom, which

had been present for four weeks, was sometimes relieved by belching. He had no symptoms indicative of cardiac weakness. He had marked enlargement of the axillary lymph nodes and physical signs indicative of an infiltration of the left pulmonary apex.

Heart. Dulness extends from upper border of the third rib just below the right sternal border to one finger's breadth outside the midclavicular line. There is a marked presystolic thrill. On auscultation at the apex a rumbling presystolic sound is heard, ending in a loud booming systolic sound. The pulmonic second sound is greatly accentuated. The temporal arteries are sclerotic, the radial pulse has a small volume, that on the left being smaller than that on the right.

On further examination, an area of dulness above the heart and to the left of the sternum was discovered, which suggested the existence of an aortic aneurysm.

Laryngeal Examination (Dr. Singer). Complete paralysis of the left vocal cord, without any other signs of local abnormality.

X-ray Examination (Dr. Pancoast). The heart is enlarged after the manner indicated by the physical examination. The bronchial lymph nodes are enlarged.

Later on the patient developed cough when in the recumbent posture. The heart became more dilated, and the presystolic murmur less loud. About this time he became confined to bed, his symptoms having progressively increased in severity. His private physician and a consultant, on being called to see him, pronounced his case one of thoracic aneurysm with cardiac enlargement. Death occurred as the result of edema, dyspnea, etc. No autopsy was held.

Of all internal maladies, disease of the aorta is most frequently the cause of left recurrent laryngeal paralysis. Among 69 such cases Syllaba found 17, while Guder and Dufour encountered 8 cases among 79 (2 of complete paralysis and 6 of paresis) due to this cause. In 1 of Ortner's and in 1 of Osler's cases aortic aneurysm had been diagnosticated, and not unnaturally, since disease of the aorta and mitral stenosis may have many symptoms in common, among which inequality of the radial pulses and anisocoria,[1] cya-

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[1] Harris, Harveyian Society, London, 1903.

nosis, cough, dyspnea, aphonia, and pulsation in the second left intercostal space may be especially mentioned. Indeed, Boinet has suggested that periaortitis may cause a recurrent paralysis by direct extension without any compression whatever. It is also possible that antecedent infections, especially diphtheria, may give rise to the vocal paralysis. Chronic adhesive pericarditis, which was found in 3 of the reported cases, might readily account for the nerve paralysis. In Herrick's case the left recurrent laryngeal nerve was embedded in a mass of cicatricial tissue.

The cases reported by Gantz and by Palasse were in all probability also the result of glandular pressure, a process in which it is incredible that the heart should have played any part. Pulmonary tuberculosis may cause recurrent paralysis either by direct glandular pressure—a gland is normally found between the bronchus anteriorly and the nerve posteriorly—or as the result of pleuritis, or through involvement of the pericardium or pulmonary consolidation. The knowledge of these facts makes one distinctly skeptical of the accuracy of Ceraulo's observations of twenty cases supposedly due to mitral stenosis. Quadrone reports eight cases in which paresis or paralysis of the cords occurred in cases of mitral disease, without any changes in the laryngeal mucosa, without any demonstrable cause other than the heart lesion. Three cases were examined with the x-rays. The reports of Syllaba, Alexander, Gavello, Quadrone, Perotta, Sheldon, Guder and Dufour, Pallasse, Pal, Ceraulo, Mead, Dmitrenko, and Koellreuter, being unsubstantiated by autopsies, leave us in much uncertainty as to the actual mechanism of the compression, though they seem sufficient to emphasize the relationship of the two pathological conditions.

The observations of Ortner to the effect that the pressure was exerted by the left auricle against the left bronchus in one case and against the aorta in the other, would seem to be faulty. To have the auricle press upon the aorta would necessitate that the pulmonary artery unguard the nerve by being thrust not only backward but downward and away from the aorta in a manner and to a degree that is practically inconceivable. As regards pressure upon the trachea by the auricle, it is anatomically impossible to have the

recurrent laryngeal nipped between the left auricle and the bronchus. This statement is made despite the fact that both King and Friederich[1] have reported compression of the left bronchus by a dilated left auricle, an entirely different matter, and occurring below the lowest part of the recurrent laryngeal loop. These errors, like many others, tend to support the belief that the ordinary method of performing autopsies will not reveal the minutiæ of interrelational thoracic anatomy. Only by having the body hardened before it is studied can such intimate details be determined with exact definiteness.

Kraus' explanation of the mechanism at work has more to commend it, although he is in error in regard to some of his anatomical relations. In addition to marked dilatation of the left auricle, he ascribes some of the trouble to a hypertrophied right ventricle, with consequent alteration of the relations at the aortic arch. He states that in his case the aortic ligament, instead of running upward and to the left, ran more horizontally. As a matter of fact, the abnormal course described by Kraus is the normal one. However, the ligament may have been more horizontal than usual, and this was probably caused by a pushing up of the pulmonary artery and not by a pulling down of the aorta.

In this connection it should be stated that the possibility of traction on the aorta by the pulmonary artery through the medium of the ligamentum arteriosum can hardly be looked upon seriously. The ligament runs anteroposteriorly and slightly upward, and before any downward traction could begin to be exerted the pulmonary artery would have to descend from 1 to 2 cm. It does seem a bit fanciful to assume that a structure but 2 to 3 mm. in diameter could pull downward the arch, supported as the latter is at both ends, and held up not only by the great vessels which arise from its convexity, but also by the attachment of the deep cervical fascia to the pericardium. These would certainly counteract any possible pull exerted by the ductus, to say nothing of the aid afforded by the areolar adhesions of the aorta to the adjacent mediastinal structures.

[1] Quoted Huchard, Maladies du Cœur, 1905, iii, 522.

Observer.	Age.	Sex.	Cardiac lesion.	Autopsy findings. Remarks.
Ortner, Wien. klin. Woch., 1897, No. 33	17	M	Double mitral and tricuspid; obliterative pericarditis	Nerve compressed between auricle and left bronchus; nerve discolored.
	34	F	Double mitral and aortic; tricuspid insufficiency	Nerve compressed between left auricle and aorta; nerve flattened, constricted in spots and discolored.
Herrick, Chicago Med. Recorder, 1898	38	M	Mitral stenosis; obliterative pericarditis and pleuritis	Nerve embedded in cicatricial tissue "and wedged between aorta and enormously enlarged left auricle that had forced its way in between the aorta and pulmonary artery, considerably distorting the normal anatomical relations of the parts;" nerve flattened, narrow, and attenuated, and on microscopic examination was found degenerated; auricles greatly dilated.
Kraus, Verhandl. d. XIX Kongr. f. inn. Med., 1901, p. 607	21	F	Double mitral; tricuspid insufficiency; slight aortic stenosis	Heart displaced by hypertrophied right ventricle, altering relationship of aorta, aortic ligament and pulmonary artery, with resulting traction on the nerve.
v. Schrötter, Zeit. f. klin. Med., 1901, p. 160	15	F	Double mitral, tricuspid insufficiency; patent ductus arteriosus; dilatation of pulmonary artery	Nerve compressed between origin of ductus arteriosus and aorta; constricted and discolored; trunk of pulmonary artery larger than ascending aorta, its two branches larger than normal; ductus arteriosus as large as the latter.
Hofbauer, Wien. klin. Woch., Oct. 9, 1902	32	M	Mitral stenosis	X-ray findings identical with those of Firschauer; no autopsy.
Syballa, Sem. Méd., 1903, p. 44	47	M	Mitral stenosis	No autopsy.
Sheldon, Medical Rec., Nov., 1904	38	F	Mitral stenosis	No autopsy; vocal cord paralysis appeared and disappeared with broken compensation and improvement respectively.
Quadrone, "le paralisi delle corde vocali nei vizi mitralici," Scritti Medici in onore di C. Bozzolo, 1904, p. 515	..	F	Mitral stenosis and insufficiency	No autopsy notes; bilateral paresis; nerve histologically normal.
	..	F	Mitral stenosis	No autopsy; bilateral paresis.
	..	F	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	F	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	M	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	F	Mitral stenosis	No autopsy; bilateral paresis.
	15	F	Mitral stenosis	No autopsy.
	..	F	Mitral stenosis and insufficiency	No autopsy; left rec. paralysis.
Alexander, Berlin klin. Woch., 1904, p. 135	50	F	Mitral stenosis	X-ray findings identical with those of Firschauer; no autopsy.
Firschauer, Wien. klin. Woch., 1905, p. 1383	30	F	Double mitral; tricuspid insufficiency	Nerve compressed between left pulmonary artery and aorta by forward and upward pressure of dilated left auricle and pulmonary vein.
Trétrop. Bull. de la Soc. belge d'otolaryngologie, 1905, p. 180	49	M	Mitral insufficiency	No autopsy; paralysis appeared and disappeared as patient got worse or better.
Hofbauer, Wien. med. Gesellsch., Nov. 14, 1905	30	M	Mitral stenosis	Nerve compressed between left auricular appendix and aorta, the former being pushed upward between the pulmonary artery and aorta.
Pal, Sem. Méd., 1905	..	..	....	No autopsy; brief verbal report.
Bonardi, Gazz. Med Italian, 1906, p. 41	40	F	Double mitral tricuspid insufficiency; pericarditis	Nerve compressed between aorta and enormously dilated left auricle.
Koellreuter, Monatssch. f. Ohrenheilk., 1907, p. 1	29	F	....	No autopsy; x-ray, tracheoscopic, and esophagoscopic examinations; mediastinal neoplasm; points out fallacy of accepting non-autopsied cases.

TABULATION OF REPORTED CASES—*(Continued)*.

Observer.	Age.	Sex.	Cardiac lesion.	Autopsy findings. Remarks.
Zimbler, Thèse de Balc, 1907	25	F	Congenital pulmonary stenosis and insufficiency; patulous ductus arteriosus	No autopsy; *x*-ray examination similar to that in v. Schrötter's case.
Gavello, Bull. di Malattie di Orechio, Nov., 1905	19	F	Mitral stenosis	No autopsy; *x*-ray excluded possibility of disease of the aorta.
Ceraulo, M o r g a g n i, 1907, No. 6	..	..	....	No autopsies; claims to have seen 20 cases in mitral disease, of which two were stenosis; no details.
Perotta, Arch. Ital. di Laryngol., 1909,p.71	38	F	Mitral stenosis	No autopsy; tertiary syphilis.
Guder and Dufour, Rev. de Méd., 1909, p. 300	43	F	Double mitral	No autopsy; partial paralysis; *x*-ray examination.
Osler, Arch. de Mal. du Cœur, 1909, p. 74	24	M	Double mitral	No autopsy; adhesive pericarditis?
	45	F	Mitral stenosis	Nerve compressed between left auricle and aorta?
	27	F	Double mitral	No autopsy.
	48	M	Double mitral with aortic insufficiency	Nerve compressed between left auricle and aorta. It was white and sclerotic; auricle size of small fist.
Boinet, Bull. de l'Acad. de Méd., 1910, p. 211	23	F	Mitral stenosis	No autopsy; paralysis appeared and disappeared as heart action became worse or better.
	25	F	Double mitral	No autopsy; *x*-ray showed great auricular dilatation, the aorta being apparently normal.
Pallase, Lyon Médicale, 1909, p. 719	20	F	Mitral stenosis	No autopsy; pulmonary tuberculosis; mediastinal adenitis revealed by *x*-ray.
Mead, Jour. Am. Med. Assoc., 1910, lv, 2205	..	F	Patulous ductus arteriosus; aortic and mitral stenosis; coronary and aortic sclerosis	Exact mechanism not stated; compression presumably due to dilatation of pulmonary artery which was distended to twice the size of the aorta; recurrent laryngeal nerve both macroscopically and microscopically normal.
Dmitrenko, Rousskyi Vratch, 1910, No. 1; Abs. Arch. de Mal. du Cœur, Jan., 1911, p. 48	29	M	Mitral stenosis	No autopsy; paralysis attributed to dilatation of pulmonary; artery; tracings were taken from same in the pulsating second left intercostal space; *x*-ray showed left auricular enlargement.

The obliterated ductus arteriosus is mentioned frequently in the autopsy records. It is our opinion that this structure is a factor of minor or even negligible importance, its main and perhaps only influence, aside from its mere presence, being to hold in approximation to a very slight degree the aorta and the left pulmonary artery. Even should the ductus be patulous, it does not follow that it has any intrinsic influence. We are inclined to believe that in these cases, such as v. Schrötter's and Mead's, the two factors of immediate significance are identical with those in which the ductus is obliterated, viz., the aorta and the left pulmonary artery, the patu-

lousness of the ductus being of importance only on account of the associated dilatation of the pulmonary artery and the engorgement and hypertrophy of the right ventricle.

SUMMARY. There are now on record 11 autopsied and 26 clinically reported cases in which recurrent laryngeal paralysis was associated with and apparently the result of mitral stenosis. Among the autopsied cases the vocal paralysis was attributed to direct compression on the part of the auricle or its appendix in 7; to cardiac displacement, traction, etc., in 1; to the effects of a persistently patulous ductus arteriosus in 2; and to indirect compression acting on the pulmonary artery in 2.

CONCLUSIONS. It is our conviction, based on careful study of the anatomical relations in hardened preparations, that the indirect mechanism may be a variable one, but that when compression is accountable for the recurrent paralysis, it must always be caused by the nerve being squeezed between the left pulmonary artery and the aorta or the aortic ligament.

Anything which will dilate or force upward the left auricle, the left upper pulmonary vein, or the left pulmonary artery would tend to cause the condition.

The anatomical relations are such that direct pressure of any portion of a dilated left auricle upon the aortic arch is impossible.

When we consider the softness of all the structures involved, and the fact that the nerve is normally flattened against the aorta, not rounded, it would seem probable that its function is abolished, not from actual destruction from pressure, but from a neuritis consequent upon a degree of compression which could hardly be sufficient to actually destroy the vitality of the nerve. This, of course, can be determined only by microscopic examination of the nerve.

DISCUSSION.

Dr. John H. Musser: I should like to ask if we must not consider that the pressure against the aorta spoken of was not similar to the action of pressure against a cushion? One would hardly think that the pressure under such circumstances would be sufficient, unless there was actual disease of the aorta also, to bring about such change in the nerve trunk.

Dr. Fetterolf, closes: That is a question which we cannot answer categorically. Dr. Norris found one case on record in which at autopsy there were in the left auricle 3000 c.c. of blood. This illustrates the amount of distention and possible pressure which can be brought to bear, and we believe that compression can and does account for the nerve paralysis. The fact that in some of the cases the paralysis appeared and disappeared as compensation failed or was restored is confirmatory of pressure as a cause.

CHRONIC PANCREATITIS: ITS SYMPTOMATOLOGY, DIAGNOSIS, AND TREATMENT.[1]

BASED ON A STUDY OF THIRTY-EIGHT CASES.

By JOHN B. DEAVER, M.D., LL.D.

In the domain of pancreatic disease there still remains much unbroken ground. Uncertainties in pathology, obscurities in symptomatology, and difficulties in diagnosis beset us and render our clinical judgments difficult and our therapeutics far from satisfactory. Only by the accumulation of accurate observations can the subject be cleared up, and it is desirable that each should add his personal experience. With this in mind I have reviewed those cases of chronic pancreatitis which have come under my personal observation during the last few years and of which my records are sufficiently complete to warrant their inclusion. For the laborious task of collecting and analyzing the cases I am indebted to two of my house doctors, L. C. Kinney and Le Fevre Stewart, and to my assistant, Dr. D. B. Pfeiffer.

Of the various affections of the pancreas, those composing the group due to inflammation and its sequels are the most frequent and important. By reason of its protected situation, direct injuries to the pancreas are uncommon. Likewise, while it is subject to the various neoplasms affecting parenchymatous organs, there is no such tendency toward tumor formation as occurs in certain other parts of the body. The observations of recent years, however, made chiefly at the operating table, have made it apparent that inflammatory changes are much more frequent than anyone had hitherto surmised. It was but natural

[1] Read March 1, 1911.

that the most extreme grades of inflammation were the first to claim attention, and since the pioneer work of Fitz the acute and subacute forms of pancreatitis have been clothed with a fairly definite pathology and symptomatology, though it is but just to say that our knowledge even here lacks completeness; and in the individual case the difficulties are many.

It is, however, when we approach the consideration of the lesser degrees of inflammatory change of chronic nature with their less characteristic clinical declarations, that we feel our ground often slipping and insecure. Fitz wrote understandingly of chronic pancreatitis, and the chief additions to our knowledge since then have been made by Körte, Oser, Lancereaux, Opie, Moynihan, Robson, Cammidge, Truhart, and Lazarus. Still most clinicians are agreed that the diagnosis of chronic pancreatitis is exceedingly difficult. The extremes of opinion in this respect are those of Opie, who holds that "the lesion is seldom associated with such definite symptoms that it is recognizable during life," and of Robson and Cammidge, who state that, "from the information obtained by a careful examination of the patient, a knowledge of the history of the case, and the results of a chemical and microscopic examination of the excreta, a correct opinion may be formed in a large majority of instances." My own feeling in regard to this matter is located somewhere between these pessimistic and optimistic expressions. Certainly the diagnosis has been made a sufficient number of times to demonstrate that it is not too difficult to attempt; but it is equally true that our present criteria are too uncertain and inconstant to warrant a claim for great accuracy. We must aim to improve our methods and our understanding. There are no pathognomonic symptoms, no short cuts to the diagnosis of chronic pancreatitis. It is to be made only by the solution of an equation, the factors of which are obtained by three separate lines of inquiry, viz.:

1. The anamnesis.
2. The physical examination.
3. The special tests designed to show disturbances of pancreatic function.

I have divided my cases into two groups, according to the presence or absence of gallstones. Of the 73 cases, in 35 there were stones in some portion of the biliary passages, and in 38 there were none at the time of operation.

In these remarks I shall restrict myself to the non-calculous group, believing that these cases will give a truer picture of pancreatic disease *per se.* The cases with stones will be considered at another time. The series is still not entirely pure, since 12 had demonstrable changes in the gall-bladder at the time of the operation. Hence a certain admixture of biliary symptoms may be present in this analysis.

A careful history is of the first importance. Habits of eating or drinking which set up chronic inflammatory changes in the stomach and duodenum will be found in certain cases; in others a history of the infectious conditions which are especially likely to be followed by disease of the biliary passages. Often a history of antecedent, disregarded, and perhaps forgotten indigestion is obtained. If disease of the bile ducts and gall-bladder have preceded the pancreatic inflammation, the early history will partake of the inaugural symptoms of that disorder, and perhaps frank attacks of hepatic colic have occurred.

The relation of sex to chronic pancreatitis as compared with cholelithiasis is reversed. There were 22 males and 16 females. This corresponds with Opie's figures, who found 17 males and 13 females. Bohm's large statistics also show that 65 per cent. occurred in the male sex. In view of the preponderance of biliary infections in the female sex, this fact is significant as showing that there must be some essential difference in the factors which produce infection in the ducts of these closely situated viscera. According to Desjardins, the same infection arising in the intestine and travelling up the bile and pancreatic ducts will, in the former situation, induce a stone-forming catarrh, but in the pancreas will cause a chronic interstitial inflammation. The lack of parallelism in the two kinds of infection, while not conclusive, creates a presumption against such complete similarity of origin in the majority of instances.

The incidence according to age is as follows:

Below 30 years	4
30 to 40 "	11
40 to 50 "	11
50 to 60 "	8

More than two-thirds of Opie's cases occurred between the ages of forty and sixty. In my series it is seen that the age is lower, two-thirds occurring between the ages of thirty and fifty. This is accounted for by the fact that all but one of my cases were operative, while Opie's statistics include postmortem records.

The onset of symptoms is spoken of as sudden in 25 cases, gradual in 13; but these figures refer especially to exacerbations, premonitory symptoms being present in the majority of instances.

The leading and most constant symptom is pain, which was absent in only 3 cases. I am conscious of the fact that I am dealing with a series of cases that have been driven to surgical intervention. This magnifies the importance of pain as a symptom, for too frequently it requires suffering to bring a patient to the operating table. The practitioner must see many cases of pancreatitis in which pain is absent or inconspicuous.

The pain of chronic pancreatitis, or its mild exacerbations, is not in itself characteristic. It varies from dull discomfort or ache to sharp lancinating or colicky pain quite like gallstone colic. It may be merely a sense of fulness or oppression in the epigastrium. The pain was severe in 12 cases; moderate in 21; in 11 it was colicky.

In the majority of cases when the pain was colicky in type the gall-bladder was diseased. In one instance several small stones had been passed *per vias naturales* a short time before, though none was found at the time of operation. It seems probable that by the dilatation of the ducts following passage of a stone, the gall-bladder had been enabled to empty itself of its calculous contents. From these observations I am inclined to interpret colicky pain, when present, as evidence of involvement of the bile passages. In 17 cases the pain was located in the epigastrium; in 15 beneath the right costal margin; in 1 beneath the left costal

margin; in 2 it was lumbar, and in 1 severe exacerbation it was general. From the primary location radiation took place to the epigastrium in 5; to the back in 9; to the right and left costal margin in 8 and 1 cases, respectively, and to the right and left shoulders in 9 and 2 cases, respectively.

No definite relation to eating or to any particular articles of food was brought out in this series. This seems to be of some value in differentiating pancreatic pain from that of ulcer of the stomach or duodenum and, to a less extent, from gall-bladder disease.

It has been observed that in some cases the carbohydrates are most likely to set up digestive disturbances, and Sailer found that the administration of glucose for the purpose of testing the assimilation limit was particularly distressing to these patients.

But slightly less frequent than pain is the history of nausea or vomiting or both. Twenty-one of my patients had had attacks in which vomiting figured, while 10 more had been nauseated without actually vomiting. Opie has called attention to the association of chronic interlobular pancreatitis and persistent vomiting, and cites 4 of his 30 cases, in which advanced chronic interstitial inflammation was found in individuals who during life had suffered with persistent vomiting. While I have not encountered vomiting lasting persistently over a considerable period of time, yet the prominence of nausea and vomiting occurring in attacks at variable intervals indicates its importance as a symptom of the more severe type of the disease.

In 10 cases it occurred before the onset of actual pain. This may have been due to what Mayo has spoken of as "the association of surgical diseases in the upper abdomen," for we must always remember that pancreatitis is a disease which in the majority of instances is preceded by, or associated with, disease of the neighboring organs, such as gastritis, duodenitis, or biliary catarrh. The vomiting of pancreatitis is non-characteristic, though often containing mucus and bile. Eructations of gas are common in this disease as in most other abdominal affections, and were specially mentioned as a distressing symptom in 12 cases.

The third important symptom is jaundice. This also, as a striking and intensely disagreeable thing for the patient, like pain, is apt to be magnified in importance in any operative series. It was present at the time of operation, or previously in 24 cases, absent in 14. Eleven patients were jaundiced when admitted. The mechanism of the production of jaundice is easily understood when it is considered that the common duct, in approximately two-thirds of all cases, courses through the head of the pancreas before reaching the duodenum. As this is the portion of pancreas which is most commonly affected by inflammation, it is to be expected that biliary drainage in a percentage of cases will be interrupted by tumefaction of the tissues embracing the duct. It is certain that many cases of so-called catarrhal jaundice are to be explained in this manner.

Owing to this inconstant relation of the choledochus to the pancreas, it is apparent also that a high degree of inflammation or sclerosis of the pancreas may be consistent with the absence of jaundice. All the cases of jaundice with pancreatitis are not to be explained on mechanical grounds, but a certain percentage are doubtless due to disease of the bile passages themselves or to extension of inflammation from a catarrhal duodenum. The jaundice may come on painlessly, as occurred in 4 cases. It may also be continuous, as in 5 cases. The surgical importance of these facts cannot be overestimated. When associated with rapid wasting and loss of strength, which may occur in this disease, the clinical simulation of malignant disease of the head of the pancreas is complete and patients have repeatedly been denied operation under the impression that it was useless; a fatal blunder. Here also I may say that the mistake is not always rectified by simple exploratory operation, for the hardened nodular pancreas of advanced inflammation may so resemble carcinoma as to defy differentiation by direct inspection and palpation. Even the glands of the neighborhood may be greatly swollen, as though by extensive metastasis. Robson, Moynihan, Mayo, and other leaders in upper abdominal surgery, have more than once mistaken inflammation for carcinoma, and I own to the same error

on a number of occasions. In one case not only was jaundice
and wasting present, but there was marked ascites due probably
to the biliary cirrhosis or to pressure of the thickened head of
the pancreas on the inferior vena cava. The patient made a good
recovery after operation.

I have in mind now a physician of this community on whom I
operated within the last year and closed with a hopeless prog-
nosis of pancreatic carcinoma. The subsequent course has led
me to believe that in this case I was deceived.

More often jaundice is preceded by pain as in gallstone colic,
though, as previously stated, the pain is apt to be less severe and
not colicky in character. In the more acute forms of pancreatitis
it is, of course, a well-known fact that the pain is of such agonizing
severity as hardly to be compared with that of any other disease.
Such an exacerbation may occur at any time in the course of
chronic pancreatitis.

The combination of intermittent jaundice, pain, and febrile
attacks may also be perfectly characteristic of Charcot's hepatic
intermittent fever. I have diagnosticated stone in the common
duct in such cases, and when considering them later have been un-
able to find any reason why I should not do so again. I am not
sure that a stone may not have been present and escaped shortly
before operation, and I have referred to one instance above in
which such was known to have been the case.

The degree of jaundice may vary from the slightest tinge to
the "black jaundice" of the older writers, which was supposed to
be diagnostic of malignant disease. Sialorrhea, though often
mentioned, I have not observed.

General symptoms are usually well marked. The existence of
chronic pancreatitis, to a degree that pancreatic function is seri-
ously disturbed, is always associated with a loss of weight. This
is due to several causes: First, to a restriction of the diet volun-
tarily or by advice of physician in the effort to control the symp-
toms of indigestion. At times impairment of the appetite is
responsible for decreased intake of food, though loss of appetite
is by no means a constant accompaniment of pancreatitis. In

this series it is mentioned seven times. There is also no disgust for meat. The persistence of the appetite is a valuable point of difference from carcinoma. Second, it is due to malassimilation of the imperfectly digested food. Third, in the cases in which jaundice is present, to the influence of the biliary intoxication; and finally, in a few cases, to the absorption of the products of bacterial activity.

Loss of weight was noted in 21 cases. The state of nutrition at the time of operation was, in 6 cases, obese, in 10 good, and in 13 poor. Loss of strength follows loss of weight, and was complained of in 10 instances. I have already referred to the rapid loss of weight and strength which may take place in some instances, particularly when jaundice is a marked symptom. The cachexia may be as rapid and extreme as in malignant disease. In the usual case such marked wasting does not occur.

In most instances fever was known to have been present, and in 5 a history of chills and sweating was obtained. In 1 the temperature was slightly subnormal. In 11 at the time of operation it was between 98° and 99° F., in 13 between 99° and 100° F., and in 4 between 102° and 103° F. Fever is not such a prominent symptom in the prolonged course of chronic pancreatitis as most figures would seem to indicate. As a rule, the temperature is normal. Fever is present only during exacerbations. Between the attacks there may be non-commital indigestion. In 13 cases of this series there was indigestion between attacks. The longest duration of the disease as estimated by symptoms was seventeen years; the shortest eleven days. Ten had had frequent attacks of varying severity.

The bowels, as a rule, are constipated. Nineteen patients suffered with chronic constipation, and in 13 cases constipation was a feature of the attacks. In only 5 was there a history of diarrhea.

From this it will be seen that caution must be used in employing as an aid to diagnosis the classical description of "frequent bulky motions, pale in color, offensive, and obviously greasy." As stated by Robson and Cammidge, such stools are present only in advanced conditions.

The physical examination rarely affords much positive information. It is of more value in excluding other abdominal conditions. During exacerbations there may be epigastric tenderness and rigidity. When this is true it is almost impossible to detect anything in the nature of a mass. During the intervals, in patients with thin flaccid abdominal walls, it is sometimes possible to palpate the swollen head of the pancreas. In 3 cases of this series a rather indefinable mass could be felt. More often a considerable degree of pancreatic swelling and sclerosis will defy appreciation through the body wall and overlying viscera. In the majority of instances the pancreas is well covered by the adjacent organs. Körte, who examined 30 cadavers with reference to this point, found that in 20 the pancreas was completely covered, while in 10 some part of the gland was covered only by omentum. In 6 instances there was ptosis of the colon, with exposure of a portion of the head of the pancreas between the colon and liver. In two bodies it was exposed in the median cleft of the liver, and in 2, which were the seat of marked gastroptosis, the pancreas could be palpated directly beneath the gastrohepatic omentum. In palpating through the body wall, however, these slight exposures of pancreatic tissue are rarely sufficient to give a definite sense of mass even to the tactus eruditus.

As most of these patients were operated on during or just after some exacerbation of symptoms, there was a degree of tenderness present in most of them. In 8 no tenderness was elicited. In the remainder tenderness was found below the right costal margin in 20; beneath the left in 3; in the mid-epigastrium in 11; over Mayo-Robson's point in 3, and in 1 more severe case it was general. Rigidity was observed in the right hypochondrium in 9 cases and over the epigastrium in 3. There was moderate distention in 6 cases.

Enlargement of the gall-bladder has been observed in a number of cases, but it was not felt prior to operation in this series. The liver, however, was noted as enlarged nine times.

The general examination at times may reveal loss of weight and jaundice as above stated.

The blood frequently shows a secondary anemia which is seldom grave. In about one-half of my cases the hemoglobin was below 80 and the erythrocytes below 4,000,000 per c.c. A moderate leukocytosis was present in a few of the more acute exacerbations. Generally the numerical ratio of the leukocytes was unaltered.

Now as to the various tests used to determine the functional activity of the pancreas and upper digestive tract: A gastric analysis was made in 24 cases. In two-thirds of these there was subacidity both of free hydrochloric acid and total acids. In no case was there a marked hyperacidity. In other respects the analysis was not abnormal. The great number of conditions associated with subacidity of the gastric contents deprives this observation of any diagnostic value.

Somewhat more information can be derived from examination of the stools. In 10 instances they were clay-colored. It is well known that this characteristic does not depend so much on the absence of bile as on the presence of an excess of fatty acids or fat itself. The tests for stercobilin were positive in all of these instances, showing that bile was entering the intestinal tract. This is important and leads to the deduction that since the liver is functionating, the failure to digest the fats must be due to deficiency of the pancreas. An excess of neutral fat so marked as to be visible to the naked eye, i. e., steatorrhea, was present in only 6 cases, and an excess of soaps was found in 5 cases. In pancreatic disease the total amount of unabsorbed fat may reach 50 to 60 per cent. in cases of chronic pancreatitis, and even 75 to 90 per cent. in cases of malignant disease (Robson and Cammidge). Carnot says that after suppression of the bile alone the feces contain 60 per cent. of fat; after suppression of the pancreatic secretion, 70 per cent. of fat; and after suppression of both bile and pancreatic juice they contain 90 per cent. of fat. In health, according to Müller, "the unabsorbed fecal fats consist of approximately 20 to 30 per cent. of neutral fat and from 70 to 80 per cent. of split fat, which is partly fatty acids and partly soaps." R. Gaultier has shown that in cases of suppression of the bile there are found in the feces from 35 to 45 per cent. of

the ingested fats; 63 per cent. of this exists as neutral fats, and 35 to 40 per cent. as split fats (21 per cent. as fatty acids, and 12 per cent. as soaps). He has found that, in cases of suppression of the pancreatic functions, 80 per cent. of the fecal fat is in the form of neutral fats, and only about 15 per cent. as split fats (10 per cent. as fatty acids, and 5 per cent. as soaps); and if both biliary and pancreatic secretions are absent, 90 per cent. of the ingested fat is recovered from the feces, of which 90 per cent. is in the form of neutral fats, and 11 per cent. as split fats (10 per cent. as fatty acids, and 1 per cent. as soaps). Müller found that in cases of pancreatic disease, even though the total percentage of fecal fat might not be increased above the normal, yet the proportion of split fat is always decreased (averaging about 40 per cent. of the total fat), showing decrease in the digestive power for fatty food. It has been asserted by Katz that diminution of the split fat below 70 per cent. of the total fecal fat invariably signifies disease of the pancreas, except in nursing infants and patients with profuse diarrhea. It remains to be seen whether the quantitative relations of the fat and its derivatives in the feces will be of any great assistance. Since we have found practically normal stools in cases which presented very definite chronic pancreatitis, it is evident that a negative finding is not conclusive. Positive results, on the contrary, must be regarded as very suggestive, and the examination of the feces for its fat and bile contents constitutes a very important element in the diagnosis. Excess of muscle fibers could be found in those instances of palpably deficient pancreatic function, but was not a characteristic of this series. The digestion of protein material appears to be less helpful than fat digestion. Fitz has pointed out that the condition occurs "only when there is extreme diminution of the pancreatic juice, and is significant only when gastric digestion is normal, when the diet contains no excess of meat, and when there is no diarrhea" (Opie). In fact, the majority of stools showed nothing by which a presumptive diagnosis of lack of pancreatic secretion could be assumed. As Opie remarks, "in most instances a considerable part of the parenchyma is undestroyed, and is capable

of performing, in part, at least, the functions of the glands. The characteristic stool of pancreatitis, when present, is of great value in the diagnosis, but when absent does not negative the existence of pancreatitis.

The examination of the urine has been given special prominence by the reaction of Cammidge, which has received the endorsement of such able surgeons as Robson and Moynihan. As is well known, this reaction consists in the demonstration in the urine, when treated by a rather complex chemical procedure, of certain crystals of a definite morphology and certain solubility characteristics, but of unknown composition, though it is thought to be a derivative of a pentose, probably an osazone.

A positive reaction is said to indicate the presence of simple pancreatitis. It has been found in a percentage of cases of carcinoma of the pancreas, which is explained by the originators as due to the presence of an inflammatory zone about the neoplasm. The improved or "C" reaction is now used to the exclusion of the old "A" and "B" methods.

The table published in Robson and Cammidge's recent book gives the reaction credit for accuracy rarely attained by any other laboratory method.

In 67 cases of pancreatitis it was positive in every case. In 16 cases of carcinoma of the pancreas it was found in 4 (25 per cent.). On the other hand, in 50 normal cases used as controls it was uniformly negative, while in 117 associated cases, in which there was no pancreatitis, it was positive only four times. This is a remarkable showing, and if obtained by others would almost obviate the necessity of obtaining a history, a physical examination, or, indeed, seeing the patient at all. We have paid special attention to the Cammidge reaction in the German Hospital. Dr. Kinney has been especially interested in it, and his report of the first 154 "C" reactions appeared in the *American Journal of the Medical Sciences* (December, 1910). Following the cases included in his report we have had 197 additional cases, making, in all, 351, which constitutes a very fair experience by which to judge the merit of the test. While I am free to admit that the

originator of the reaction can probably perform it best, yet his very detailed directions have been most carefully followed, and our results must certainly approximate the best obtainable under similar circumstances.

Of 19 cases, in which the test was made in the present series, it was positive in 4 and negative in 15. This is a scarcely higher percentage of positives than we obtained in 60 cases in which the pancreas appeared to me to be normal to direct palpation at the time of operation. Ten of these 60 cases gave a positive Cammidge reaction. One-fifth positive in pancreatitis, as compared with one-sixth positive when no pancreatitis existed, does not inspire faith in the reaction. In 55 cases of chronic pancreatitis, confirmed at operation, some of which were complicated by other upper abdominal disease, there were 18 positives (32 per cent.), a slightly better showing. Two acute cases were both positive. One case of pancreatic cyst was negative; one of pancreatic fistula was positive, and of 8 cases of carcinoma of the pancreas, one-half gave the reaction. Roughly speaking, in all my cases in which the condition of the pancreas was determined accurately at the time of operation, this supposedly specific pancreatic reaction was obtained only about two and a half times as frequently when the pancreas was affected as when it was not. While this speaks for a degree of dependence on pancreatic disease, it does not, to my mind, indicate that that relation is by any means so intimate and constant as we had been led to hope.

The urine in suspected pancreatitis should be carefully tested for bile and sugar. Two cases in this series showed glycosuria. Sugar may appear in the urine during an exacerbation and clear up on subsidence of the inflammation. This is a threat of oncoming diabetes, and should not be overlooked.

I have not used the Loew pupillary reaction, which consists in a dilatation of the pupil on instillation of epinephrin into the conjunctival sac. This is supposed to be due to some interrelation between the product of the suprarenal capsule and the hypothetical internal secretion of the pancreas. Clinical reports do not accord it much value.

Nor have I had experience with the various methods of obtaining duodenal juice, either through the stomach or in the feces, and testing it for the presence of pancreatic ferments. It seems to me that as these ferments act in incredibly small quantities, so long as there is any pancreatic tissue functionating we would expect to get the reaction due to their presence. When they are absent the condition would probably be far advanced and capable of detection by simpler means.

The chief tests of this sort are as follows: Schmidt's test depends on passing a small piece of beef, enclosed in a silk bag, through the intestinal tract, and observing whether the muscles of the fibers showed digestion. Sailer quotes the work of Steele, who came to the conclusion that this was valueless.

Müller's test aims to demonstrate the absence or presence of a proteolytic enzyme in the feces, by observing whether digestion of blood serum will take place when drops of fecal material, appropriately prepared, are placed on its surface.

Sahli's desmoid test consists in administering capsules, hardened in formaldehyde resistant to the gastric juice, but soluble in pancreatic secretion. In the capsule is placed a substance capable of rapid absorption and excretion in the urine, thus determining whether solution has been affected.

Solomon attaches great importance to the amount of lecithin in the feces, which is said to be increased in pancreatitis.

Fedeli and Romanelli have devised a test to measure the activity of carbohydrate digestion.

While it is too early to say that these tests have no value, it is not likely that they will put an end to our difficulties in the diagnosis of chronic pancreatitis.

The appetite is usually fair or quite good. If nausea or vomiting occurs without severe pain, and if remittent jaundice comes on with distress, but without characteristic gallstone seizures, the presumption is strengthened.

If the pancreas may be felt enlarged and tender, or the feces present the characteristic stool, the diagnosis can be made with a fair degree of certainty. It is often necessary to observe these

patients over a considerable period of time to come to a definite conclusion. As this early non-characteristic stage is very like the non-characteristic beginnings of some forms of malignant disease in the upper abdomen, it is necessary to be guarded in the prognosis and the decision to delay operative treatment.

The chief conditions likely to be mistaken for pancreatitis are cancer of the pancreas, of the common bile duct or the liver, gallstones in the common duct, chronic cholangitis without stones, and chronic appendicitis of the type manifesting itself chiefly or solely by upper abdominal symptoms.

The treatment of chronic pancreatitis begins with the amelioration of the predisposing cause or causes, if they can be determined. When gastroduodenal catarrh is present as a result of vicious habits of eating or drinking, a reform must be instituted in these respects. When it is associated with disease of the biliary passages, treatment should be directed toward that condition. Wohlgemuth has shown that the pancreas responds actively to a carbohydrate diet, and that if rest for the inflamed gland is desired it is necessary to be sparing in articles of that nature. Carnot is enthusiastic in advocacy of supplying the missing elements of digestion by administration of a preparation of the gland. Sailer also reports good results in two cases treated on this basis. While such measures may suffice for mild cases, or at times for more severe forms, there are others that go from bad to worse on careful medical treatment. Continued loss of weight, persistence of indigestion, recurring exacerbations, jaundice, or a lowered tolerance for carbohydrates, as shown by transient glycosuria, should cause the physician to advise operation. Especially binding is this obligation if there be associated disease of the biliary tract.

In the surgical treatment of chronic pancreatitis, Mayo Robson occupies the same position as Fitz does to the development of our knowledge of the disease. He was the pioneer in showing that free drainage of the biliary tract, and through this outlet, drainage also of the pancreatic ducts, would in many instances enable the pancreas to cast off the infection and resume its normal function. This is, in a nutshell, the principle of the treatment,

and though it may seem roundabout, its efficacy has now been
demonstrated too often to admit of a question. The easiest and
most advantageous method of providing drainage is by a chole-
cystostomy. If for any reason this is impracticable, drainage of
the common duct should be done. At times when the closure
of the common duct is complete and likely to be lasting, a chole-
cystenterostomy may be best, but as a general rule external
drainage permits subsidence of the swelling of the pancreas and
a reëstablishment of the functions of the ducts. Drainage should
be maintained for three or four weeks at least. It is difficult to
keep the fistula from closing too soon, and in cases of marked
pancreatic disease it is best to make a cholecystduodenostomy.
Just how long this opening will remain patulous is a question,
for I have reoperated in cases in which this operation had been
performed, and have found the opening closed. It should not be
forgotten, also, that cholecystduodenostomy is an operation of
greater magnitude and slightly higher mortality than simple
cholecystostomy.

The surgeon today makes the same plea for chronic pancreatitis
as he made twenty years ago for appendicitis. Send patients early
before complications create a mortality.

DISCUSSION.

Dr. Joseph Sailer: Perhaps some cases of chronic pancreatitis are
amenable to medical treatment. There must be, however, a much larger
number relievable only by surgical measures. There is certain experi-
mental evidence that medical treatment may be of avail. I refer to the
experiments of Dr. Pratt upon dogs, in which proof of this was obtained
by ligation of the pancreatic duct. He has found that these dogs exhibited
practically the same symptoms that will be found in the human being
suffering from chronic pancreatitis. To a large extent these symptoms
were abated by feeding the dogs with fresh pancreas secured from slaugh-
ter houses. The gain in weight and strength of the animals was really
in some cases remarkable.

In a paper which I read before the College last year I called attention
particularly to the great difficulty of explaining these results upon a
physiological basis. I am rather of the opinion that the carbohydrate

ferment in the pancreas is responsible, because it has been my observation, in a much more limited number of cases than Dr. Deaver reports, that the carbohydrate digestion is not as good in these cases of chronic pancreatitis as are the fat and proteid digestions.

I think it must be manifest, too, upon theoretical grounds, which I believe is confirmed by operative experience, that there are a considerable number of cases of chronic pancreatitis in which operation is necessarily of no avail. Particularly is this true in that large group of chronic pancreatitis in which the parenchyma of the pancreas is not particularly affected, but in which the islands of Langerhans are sclerosed, associated with a severe form of diabetes. I hope that perhaps these cases may be amenable to surgical treatment, because at the present time they are so absolutely hopeless in the hands of the internist.

The cases of chronic pancreatitis show great dissimilarity from the cases of acute pancreatitis. This is particularly true of the toxemia that occurs in the latter and never in the former, although in both there is apparently retention of the pancreatic juices.

In chronic pancreatitis aside from the emaciation, which can easily be explained by defective digestion of the pancreatic juices, there seems to be no general disturbance.

In those cases of acute pancreatitis with toxemia it has seemed to me desirable to discover whether there has been absorption of some particular toxin in the blood. I think that such a discovery would open up a new field for the study of pancreatic conditions. I have not felt that any of the methods that have been suggested, particularly by the German experimenters, for immunizing animals against toxins, are really of scientific importance. The results have been entirely too uncertain.

I desire to congratulate Dr. Deaver and the College upon this presentation of what I believe is one of the most difficult subjects in medicine and surgery.

Dr. John H. Musser: It will be interesting to learn from Dr. Deaver what proportion of cases presenting symptoms of chronic pancreatitis and operated upon were found to be free from pancreatic disease. Those of us who are engaged in internal medicine have not the opportunity to study "living pathology," and cannot have as accurate statistics as, of course, the surgeons, to demonstrate this proposition. We must follow the lines which Dr. Deaver has laid down in order to establish the diagnosis of chronic pancreatitis, and upon such lines I feel from time to time I have been correct in the diagnosis. On the other hand, I have felt quite uncertain at other times because of my inability to demonstrate my position.

I should like to ask whether Dr. Deaver has found in the course of chronic pancreatitis the occurrence of sudden anemias or the sudden

exacerbation of the secondary anemia that usually attends the disease. It seems to me that there is no chronic disorder in which this anemia is not more frequent than that of pancreatitic disease.

I have frequently felt that the presence of pigmentation was of value. I should like to know whether this feature, in Dr. Deaver's experience, has any significance?

DR. DEAVER, closing: I am obliged to Dr. Musser and Dr. Sailer for their discussion. I confess that I cannot see any philosophy in the medical treatment of chronic pancreatitis. I make the statements which I have in my paper without hesitancy, and I believe they are statements that any man will make if he handles 73 or 75 cases of pancreatitis in the living body.

I am familiar with the experiments my friend Sailer has spoken of, but there is a great deal of difference between the dog and the human subject.

Dr. Sailer called attention to the carbohydrate digestion, and his observations have been similar to our own. He further says that in certain cases operation is of no avail. This is quite true. These are the late cases. The time has gone by. "Now is the day of salvation." Not a week hence, or a month hence.

I quite agree with him in the hope, and I believe that the day is not far distant when the surgeon will cure diabetes. I believe, too, that diabetes is a surgical complication not belonging to the internists.

Chronic pancreatitis is due to a degree to such places as Carlsbad. We surgeons who are delving in the recesses of the abdomen know that Carlsbad brings us gallstones plentifully. If such places bring gallstones, why not the results of gallstones—disease of the pancreas.

My reason for reading this paper is to awaken an interest in my medical friends in this matter, and to ask them to come to the operating table, pay their respects to the surgeon, and learn living pathology.

Dr. Musser raised the question of what proportion of cases was diagnosticated before operation? The only certain way to diagnosticate chronic pancreatitis is to open the belly. Those of us who do not advise opening the belly are taking an undue advantage of the confidence of our patients.

As to sudden anemias, these we have not met with. We have made careful blood counts, but I am not able to verify this point. Pigmentation I have not met with.

DR. MUSSER (to Dr. Deaver): You misunderstand my question. I asked whether there were many cases of disorder, presumably due to disease of the pancreas, which upon operation were found not to be due to pancreatic disease?

DR. DEAVER (answering Dr. Musser): I would say that about one-half the cases were diagnosticated before operation.

REFLECTIONS UPON THE TEACHING OF THERA-
PEUTICS, BASED UPON FORTY YEARS'
EXPERIENCE.[1]

By H. C. WOOD, M.D., LL.D.

THE profession of medicine exists for two purposes—first, the maintenance of health, or in other words, the prevention of disease; secondly, for the alleviation and cure of pain and of disease. These two branches are in themselves distinct, and may well be spoken of as preventive medicine and remedial medicine. Concerning preventive medicine I shall have nothing more to say in this article.

Into the study of remedial medicine there enters the consideration of many sciences, both abstract and remedially practical. Among these various studies is commonly reckoned therapeutics, or that study which has for its object the application of the forces of nature, including almost every manner of natural force, mechanical, physical, chemical, and what may be known as drug force, the force which is, of course, often chemical, but very often also of a nature which is at present not understood. It is plain that therapeutics is the keystone of the medical arch, the knowledge of anatomy, diagnosis, etiology, natural history of diseases, etc., being, so far as remedial medicine is concerned, practically useful only as they subserve the purposes of the therapeutist. Of what good is it to the patient that a doctor should be able to diagnosticate to the very finest point a case of heart disease if he does not know what to do to relieve the condition and

protract life? I have in my lifetime seen many men, magnificent diagnosticians, but as doctors practically inferior because they had not acquired the knowledge and the therapeutic tact or instinct necessary for the successful use of remedies. I well remember one very famous medical professor, now transported by the gods to a wetter but to him more congenial clime, whom I often met in consultation, who would make out the diagnosis and give a statement of the condition, and the probable result of the do-nothing therapeutics which he practised, with most extraordinary skill and accuracy—but beyond this naught. As a consultant he was always, with me, most alert, intensely interested in the case, and instructive in his sayings and doings until he came to the question, "Now, what shall we do with the patient?" when he would shrug his shoulders, look around the room, and say, "Oh, you know all about that;" and that was the end of his interest.

Often, in talking with some noted doctor, I have remembered the saying of my old uncle, Prof. George B. Wood: "Show me a man who says drugs are of no value in the treatment of disease, and I will show you a man who does not know how to use them." Based on forty years' experience were these words; confirmed by forty years more of experience have they been in a second generation.

The study of what is often loosely called "therapeutics," but should be called pharmacology, consists of the study of materia medica, pharmacy, and therapeutics, including in the latter term the physiological action of drugs upon man and upon the lower animals, as well as the use of drugs in disease.

Materia medica—that is, the study of the substances used as drugs—has in the gradual specialization of medicine become largely the province of the apothecary; indeed, it is often dropped entirely from medical courses. This has always seemed to me an anomaly, for certainly to be a cultured gentleman in his profession the doctor should be able on sight to tell a ball of opium from horse dung. I believe all medical schools ought to have a short, carefully thought-out course on materia medica, in which

the student should be required to learn sufficient to enable him to go into a drug store, and not appear like an Irishman out of the bogs freshly landed in the streets of New York or Philadelphia. The study of pharmacy especially belongs to the province of the apothecary, but, on the other hand, its complete avoidance by the medical schools is at least one of the efficient causes of the extraordinary prescribing of drugs which are chemically incompatible, of mixtures that will not mix, and of the various amusing and at the same time saddening messes that are sent to be "licked into shape" by the unfortunate apothecary.

With this much of prelude I come to the consideration of the subject which is the main purpose of the present article. From this discussion shall be omitted all forms of remedial measures except medicines or drugs.

THERAPEUTICS. Previous to 1874 therapeutics had been empiric, although some of the books upon the subject had given details of the symptoms produced by the administration of various drugs to the lower animals. In 1874 I published a book in which it was attempted to put therapeutics upon a scientific as well as practical basis. The plan of action was with each important drug to discuss its influence upon man from the observed effects of small doses up to those which were capable of producing death. After this discussion the attempt was made to explain the physiological way or method in which the drug produced symptoms in man, by experiments upon the lower animals; and finally, the application of the results obtained to the practical needs of medicine, patched out, when the cloth was insufficient for the garment, by empirical knowledge. The first edition of the work sold immediately, and the final result was that in America and in the best schools of England the general plan of teaching spoken of was adopted.

In Germany there arose a school of therapeutic teaching in which comparatively little attention was paid to the effect of drugs on man, and the effort to elucidate the action of a drug was chiefly by experimentation upon animals. Most of the professors had been educated as physicians, but were especially

highly educated chemists, and taught largely from a chemical point of view, and though not all the German universities adopted this method of teaching, it may be called the German method in contradistinction to that of America and England. The effect of the German method upon the students was to produce men learned in the chemistry of drugs, learned in the symptoms and effects produced by drugs upon a half-dozen species of the lower animals, but not equally proficient in the knowledge and understanding of the effects upon healthy men, much less upon the sick. On the other hand, the American method inevitably produced men who apprehended, first, the symptoms and physiological action of drugs upon the healthy man, as worked out by legitimate experiments made upon animals and upon man, and by the records of poisoning; and secondly, by the application of this knowledge to the treatment of disease.

That the German teachers themselves who adopted what we may call the German system felt the deficiency of their method may be shown by two brief anecdotes.

The first time I ever visited Professor Schmiedeberg I was shown into his private room in the laboratory, and asked to take a seat while the *diener* went to find the professor. While waiting great was my astonishment to see, lying on the private table of Professor Schmiedeberg, a copy of my *Therapeutics*, bethumbed almost like the first Latin book of the schoolboy. Again, talking the subject over with Professor Liebreich, of the University of Berlin, he said that his position in the university did not allow him to practice medicine, but that he found it so impossible to teach pharmacology satisfactorily to himself without drug-contact with humanity, that he had started and maintained at his own expense an active and successful dispensary.

The effect of the German method upon original investigation is pronounced; the man who is trained as a chemist will naturally be more actively interested in chemical problems, and while his researches may lead to the infrequent discovery of substances of value for the relief of human suffering, after all the art of clinical therapeutics has not greatly advanced by these studies.

The science of pharmacodynamics, not correlated to clinical therapeutics, is like a sail without a boat. Perhaps no medical substance has had more ability and time spent upon it than ricinin. Therapeutically, this work has been to show that ricinin is an active poison, which is of no value in human medicine, although the expressed oil of the castor bean— *Ricinus communis*— is harmless and very useful, a fact which the little Bescherine negro knows very well as he completes his toilet by smearing his body thickly with castor oil, and then, fearless of sun or insects that bite, lies in the sand of the Soudan or Upper Egypt, naked and unashamed, pot-bellied and happy, in the sufficiency for the day of *dhurra* (Indian millet), locusts, lizards, and such ilk, and thoughtless for the morrow.

It may be permitted to an old man for once to be egotistical in using his own experiences as illustrations. Every medical research of much practical value that I have ever made has had its inspiration in the sickroom. The horrors of the sunstroke ward when I was a resident physician in the Pennsylvania Hospital, taken with the childish talk and actions of the visiting staff, led to my experimento-clinical studies, which ended in the discovery of the nature, pathology, and treatment of sunstroke, and finally to the study of fever in general, to which I chiefly owe my membership in the National Academy of Science. The clinical publications of Lauder Brunton gave rise to my paper on "Amyl Nitrite," which won the Boylston Prize. Out of the furious discussion between the various clinicians of Europe on the action of hyoscyamine, and my conclusion therefrom that there must be a much more powerful alkaloid in the crude hyoscyamine of commerce than in hyoscyamine itself, grew the discovery of the physiological and medical properties of hyoscine. First on animals, then on myself, then on my wife, then on my patients, I employed the new drug. I then gave the facts to the world. The contradictory, anomalous, and often senseless and even lethal procedures of surgeons in the treatment of the accidents of anesthesia led to my Berlin address, which brought system out of chaos and changed the treatment of the accidents of

anesthesia throughout the world. And so on to the end of the chapter.

I might go to the books for many illustrations of the point under consideration, but have used my own experience because more certain of my own mental processes than of those of other coworkers. *Ex uno disce omnes.*

The pharmacodynamist, to be useful to mankind, must be one of two things: First, a graduate of medicine, a man who is however, chiefly a physiological chemist, and Johns Hopkins University has done well to have the chair of Physiological Chemistry held by its pharmacodynamist, whose important researches, it may be mentioned, have been in physiological chemistry. The tendency of the teaching of such a professor upon the student will be to cause him to look upon therapeutics from a chemical rather than a clinical point of view, so that he will never become a strong therapeutist. Secondly, the professor of pharmacodynamics, or rather of pharmacology, may be a man who is both a pharmacodynamist and a clinician, and whose researches have been so closely connected with the daily practical work of the doctor that he alone of all men is the one to teach would-be practitioners of medicine those underlying principles of therapeutics which he has made a part of himself, so to speak, and which may make the foundation of future successful bedside work on the part of his students.

Nor rational is the division of the teaching of therapeutics into two chairs—the occupant of one of which shall be a pharmacodynamist who knows little of clinical medicine, nor by experience how a drug acts upon man; the other a professor who has never, perhaps, made a pharmacodynamical experiment upon the lower animals. He who teaches with knowledge garnered from books is a schoolmaster, not a professor. To be a professor, as I would use the word, is to be filled with practical knowledge garnered from nature or everything connected with the general subject in hand; and a professor of therapeutics should be a man who has been saturated by work in the laboratory and also at the bedside with the science and art of the treatment of disease.

The *reductio ad absurdum* of the teaching of therapeutics is found in those colleges where the professor has not studied medicine at all, and therefore can have little or no personal knowledge of the action of drugs upon healthy men, much less upon the sick, and absolutely no apprehension of the needs of the medical practitioner. The relations of bacteriology to medicine are almost as close as are those of chemistry; it may be that soon we will see a bacteriologist filling the chair of pharmacodynamics or therapeutics, as we now see the chemist. The truth is, chemistry should be taught by the chemist, bacteriology by the bacteriologist. Physiological therapeutics should be taught by a man who receives from the chemist and the bacteriologist their various products, and knows from personal experience the physiological action of these products upon animals, including man, and also knows by personal clinical experience their influence upon the sick and their special values in the treatment of disease. To such a chair should be allotted at least one assistant, well versed in physiological experimentation with drugs and the teaching of it; and perhaps a second one who has sufficient knowledge of materia medica and pharmacy, and who may be a druggist. Neither of these gentlemen should be required to devote his whole time to his respective laboratory, but allowed sufficient leisure for self-development and research.

In discussing privately the subject of the teaching of therapeutics, I have been continually met with the assertion that no human being can cover the whole that ought to be put under the name of therapeutics in the medical schools. This to me is either nonsense or evidence of the decadence of the personnel of the profession, for men are still living who have covered all these subjects thoroughly and become at the same time famous in abstract science, besides making a competence by the time the retiring age had come; and I know young men living who, I believe, can do that which has been done by their forebears—otherwise it must be that the personnel of the profession is undergoing decadence. This may possibly be true, and there are some apparent causes for such change.

Thus when I was a young man, law, divinity, medicine were the only professions; today, engineering in its various branches calls loudly and offers far more than does the practice of medicine to its followers. I believe that I would never have been a doctor had the world been in 1860 as it is today.

Nevertheless, I myself do not believe in the decadence of the profession, but it is true that there is a dearth of young men properly prepared for a professorship of therapeutics. The reasons for this are very plain: First, the man who devotes himself to therapeutics must expect very small pecuniary return for the output of labor, as eminence in this branch of medicine does not lead to consultation work nor of itself even to success in ordinary practice; secondly, because ten to fifteen years of hard, unpaying work are required for the proper preparation of the man for the chair; thirdly, because of the general lack of appreciation by the official governing powers of the requirements which the candidate for a professorship should meet. Too often there is either no chair of therapeutics in a medical college, or if such chair exist it is filled by someone who never has been properly trained for the purpose.

Once I was written to by one of the most famous therapeutists in Europe for a list of the professors of therapeutics in America. I sent him forty or fifty names. He replied: "In God's name, who are these people; I never heard of more than one or two of them."

This dearth of reputation in the therapeutic professors of the country was undoubtedly due to the fact that at that time simple clinicians were appointed to therapeutic chairs. Pure clinicians are, in truth, no more fit for therapeutic professorship than are chemists or bacteriologists.

In conclusion, I would like to say two things to those who have the appointing power in our larger teaching institutions:

1. That nothing is more stupid than the belief that forcing a man to stay in his laboratory will make him a successful research worker. If the spirit of the man is that of a pure laboratory worker, well and good; but if it requires the stimulus of contact

with disease and human misery to foster in him the desire to unravel the problems of disease, the laboratory may be but a prison-house which prevents him from gathering the materials which are necessary to his development and productiveness. I was once offered a professorship in Johns Hopkins University, with the permission to go to Europe for two years, and a salary which would have been about double that which I was receiving from the University of Pennsylvania. I refused this offer, because I recognized that unless I could practise, my life would be ruined for scientific work in medicine. With myself, at least, practically all the impulses and ideas which have been the basis of research in physiological therapeutics have come from bedside experiences.

2. I think at present too much importance is given in some of our large medical schools to the fact that a man is a discoverer of new truths; certainly, one may stand at the head of the profession and yet not be a discoverer. In his day Prof. George B. Wood was the most famous physician in the United States, not because of researches made by him, but from the fact that, having a judicial, observing, and systematizing mind, with force of character and thorough knowledge of the English language, he was able to furnish the power which forced the adoption of the *United States Pharmacopœia*, and thus brought order out of chaos in the compounding of prescriptions in the United States; to write books which were very largely used as text-books both in this country and in England, and were also in the library of almost every American physician and apothecary as practical guides; and finally was as a medical teacher the best in Philadelphia and probably in the United States. On the other hand, Brown-Séquard, whose original investigations far surpassed any previously made in America, was universally recognized as entirely unfit to be a professor. I have received from time to time, many letters, grateful and laudatory, from old students, from as far as Japan and as near as Philadelphia. In none of them, that I can remember, was anything said about my original investigations, but always of the influence which I had exerted

upon the lives of the writers by my personality and the power of my teaching.

According to my thinking, in the appointment of a professor there should be considered, first, the character and power as a teacher of the candidate; secondly, his capability of writing text-books or other books which shall have wide circulation in the general profession; thirdly, his capability of originating.

For giving a college rank among similar institutions, the amount of original work it puts before the profession is, perhaps, dominant, but neither the rank and file of the profession nor the laity know of original laboratory results unless there be made some very great practical discovery; so that for the bringing of students to a medical school it is the reputation of the teaching quality of the teachers, together with the practical monographs on disease, the systematic treatises, and the text-books written which count.

THE CONTAGIOUSNESS OF CONSUMPTION OF THE LUNGS.[1]

By ARTHUR V. MEIGS, M.D.

THE study of the disease, consumption of the lungs, or tuberculosis, as it is now more frequently called, that has been so actively pursued in the past thirty years has brought to light many things that must be valuable to the human race. If there were no other reason, this would be the case, because every sort of acquisition of knowledge and its dissemination is useful. One of the best and most valuable results of the agitation of the subject has been the establishment of institutions by private benefaction and by various branches of government for the treatment and care of persons sick with the disease. No one can appreciate the value of the modern institutions as those who remember that formerly there was no place but the almshouse for the poor consumptive, and that it was often difficult to get him admitted even there. Few arguments can be brought to bear in disproof of the claim that less people are attacked by consumption and that more recover than in former years. The reasons for this amelioration are very simple. With the progress of civilization all classes of people live more hygienically. There is less bad water drunk, and drainage conditions have been improved in a manner that is wonderful. When it is remembered also that there is less crowding, less exposure to cold, and that men in general eat better food than formerly, there is little occasion for surprise that consumption of the lungs should decrease. Humanity has been given a free rein to pursue its natural tendency toward better things, and the world has every reason to be satisfied with the result. It is my opinion that the

tendency toward hygienic living moves more rapidly when the silent force of public opinion is left to act, than when many laws are made to control it, especially if they are of a drastic character, in which case they are very difficult to enforce. Drastic health laws which prove impossible to enforce are very mischievous. They make the people impatient of authority and cause the poorer classes in particular to look with suspicion upon those who should inspire confidence and be regarded as authorities to trust in questions of health. The good that has come from the agitation of the subject of the prevention and cure of consumption is offset by some tendencies that are unfortunate and much to be deplored. The effects of these tendencies are such as to cause one to wonder whether, upon the whole, the burdens of consumptives and their families have been increased rather than lightened by the present-day agitation. However, probably the world cannot advance in any direction without causing suffering to someone, but it may be hoped that in the end the results will be wholly beneficial.

It is my desire to direct attention to things that at the present epoch are incorrectly represented, and to things that in the attempt to manage the disease and to prevent and to cure it are done that should be done differently, or left undone. It is commonly taught that it is contagious. Without making any attempt to give a final answer to the bald statement that consumption of the lungs is contagious, the question may fairly be asked whether the prevailing beliefs upon the subject are correct. There certainly is good reason to think that the danger of contagion is exaggerated and that much unnecessary fear of it exists, and that hardship and even cruelty to the sick and to their families is caused by unreasoning fear. In the *New York Evening Post*, of August 28, 1909, there is quoted an article by Dr. Beverley Robinson, of New York City, which appeared in the *New York State Journal of Medicine*. "It is a source of real sorrow to a man, as he grows older and considers carefully and calmly his professional experience, to note what harmful opinions and practice prevail," says Dr. Robinson. "Sane, conservative, well-balanced, broad-minded judgment is very frequently at a discount. It is not rarely the young man with comparatively limited knowledge and experience, but filled to an excessive degree with advanced information and

with an undue appreciation of his own value, expressed or tacitly accepted, who simply claims first place as a sort of right.

"To his predecessor, who has reached that sense which comes only as the result of many years of work and service, he yields a very small quantum, if any, of allegiance. And thus every new fad or fancy of the hour, or the day, is almost sure to meet with a certain amount of popular acquiescence. . . .

"Look a moment at what is being done about the ' white plague,' so-called. How foolish, unwise, wrong, a great deal of it all really is. Is tuberculosis contagious, or, rather, transmissible? Yes, slightly so, under certain condition, but these can very easily and with very little expense relatively, be absolutely guarded against in many instances. . . . The worst final result of all the foregoing, and very much more might be added, is to increase, in my humble judgment, 'man's inhumanity to man.'"

I have a little book entitled *Consumption not Contagious*, by Duncan Turner, Melbourne and London, George Robertson & Co., 1900. The preface to the first edition, which was published in 1894, is as follows: "The object of this little work is to dispel, or at least to combat, what are regarded by the writer as heterodox opinions concerning the contagiousness of consumption." The preface to the second edition of the book, published in 1900, contains this: "Six years have elapsed since the first edition of this little book was published. Its reception could hardly be said to have been cordial. Indeed, a well-known Sydney firm of booksellers refused to sell it or have anything to do with it, urging as a reason that it was a work calculated to do harm. How they came to this conclusion is best known to themselves, but I have every reason to believe that it has not done harm, but good, and that the book itself has been a source of comfort to many outside of my own circle of patients. Moreover, the views put forward, although in direct opposition to those accepted by the leading medical journals at the time, have been confirmed by probably the highest tribunal that was called together to consider this question. The Congress that sat at Berlin in the autumn of last year was attended officially by representatives of all the civilized powers of the world. These delegates were distinguished physicians and men of science, chosen by their respective Governments. This

Convention considered tuberculosis as a whole, but in reference to contagion they have the following resolution:

"'Tuberculosis in general, and phthisis or pulmonary tuberculosis in particular, is not "catching" in the popular sense of the word. The disease is not conveyed by the breath, nor even by coughing, except as a rare exception, nor is it caught by contact with a consumptive patient.' (Transactions of the Berlin Conference on Tuberculosis, 1899, *Lancet*, July 15, 1899.)

"That such views should find favor in the city of Koch, whose discoveries gave rise to the whole discussion, is in itself significant, and shows that the extreme opinions so much advertised a few years ago are giving way to more moderate ideas. . . .

"The additional evidence I have been able to adduce in this edition will, I trust, convince any reasonable person of the truth of my contention, especially the testimony of the medical superintendents of large sanatoriums like Falkenstein and Goerbersdorf.

"In 1898 I visited the principal sanatoriums of Germany and Switzerland, and although care was taken in all of them as regards the destruction of sputum and other precautions, not one of the superintendents believed in contagion; indeed, some went so far as to say that even the precautions that were taken were more in deference to 'advanced medical opinion' than to their own conviction on this question."

The book contains arguments which it seems to me could not fail to impress any unbiassed mind that the beliefs prevalent regarding the contagiousness of consumption are erroneous. For my own part, I am quite convinced that the word contagious is misapplied when it is in any way used in connection with consumption. To this conviction I have been driven by an extended clinical experience and by my reasoning upon such facts as I have been able to obtain from reading and from other sources. It is inconceivable to me that anyone who has ever practised medicine and has seen how measles and whooping cough, diseases which are typically contagious, arise and are propagated can apply the word contagious to consumption.

In Pennsylvania and in a good many of the other States of this country the registration of tuberculosis is by law obligatory. It is desirable to look back a few years and see what has taken

place in regard to the enactment of such legislation and what the effect has been of the attempts to enforce it. I shall confine my remarks to what has happened in Pennsylvania. Probably what has occurred here is much like what has taken place elsewhere, that similar laws have been passed and similar offices created, with officials clothed with great and I believe dangerous powers. The College of Physicians of Philadelphia is an old medical society, and an examination of the volumes of its transactions during the years that the subject of the desirability of compulsory registration was being agitated gives an interesting and instructive history of the views of a part of the medical profession at that time. This society has never taken action indorsing that of others to induce the State and city authorities to make the registration of tuberculosis compulsory. Nothing, it seems to me, could better show the folly of the enactment of legislation for compulsory registration and the futility of efforts to enforce it than two quotations that I shall give. In the annual address to the College of Physicians, delivered December 6, 1893, by the President, Dr. S. Weir Mitchell, is the following: "I feel it to be my duty as your President to call attention to the wisdom of some protest against including all tubercular disease in the list of maladies officially recognized as contagious. Even if we admit it as of this nature, it would be clear that no sufficient good could result from the extreme measure in question. Is it proposed that the Board of Health shall interfere actively in any case of consumption, and how? Is it to take cognizance of all tubercle or of all tuberculous discharge from the ear or from a gland? Where is the line to be drawn, and what protective measures are to be taken by the Board of Health? The futility of the contemplated measure is plain; it invites a form of deceit hardly to be blamed. It is so temptingly easy to consider the bronchitis of consumption as the true enemy, and elect thus to label the disease rather than to return it as tubercle to a too inquisitive Board. This is not the place fully to argue this case. It may suffice to add that our real duty at present is personally and through Boards of Health to educate opinion, and to direct and teach precautions as to antiseptic means and habits. It is but too easy to create around the consumptive a moral atmosphere of terror. For the nurse or

relative this would often be destructive of duty, and for the sick
a horrible addition to the miseries of a disease which may last for
years. . . . I trust that you will protest with energy against
any present effort to class tubercle with smallpox."

My other quotation is from the Second Annual Report of the
Commissioner of Health of the Commonwealth of Pennsylvania.
At page 26 the Commissioner, Dr. Samuel G. Dixon, in speaking
of tuberculosis, says that in 1907, "While the number of deaths
from tuberculosis was 10,825, it will be noticed that only 6109
cases were reported. This astonishing discrepancy can only be
accounted for by supposing that the medical profession is by no
means yet fully aroused to the necessity of promptly reporting this
disease. The fight against it is now fairly on, and the first essential
to a successful contest is the knowledge on the part of the Depart-
ment of every place where the foe is lurking. Without this, all
our demonstrations in the way of sanatoria, dispensaries, con-
gresses, lectures, and exhibits will represent to a great extent
time and money thrown away. The campaign will be like that
of Braddock's dress parade against the Indians, and will result as
disastrously." At page 6 Dr. Dixon estimates that "for every
death from consumption there are seven living consumptives,"
and that there were, therefore, between 60,000 and 70,000 persons
suffering with the disease in Pennsylvania in 1907. According
to the estimate of the Commissioner, only one case in ten was
reported by the physicians of the State. The two quotations tell
their own instructive story, and no very extensive comment is
required to make the lesson easy to understand. The College of
Physicians is described in its charter as a literary institution; its
President, in a dignified address displaying knowledge of human
nature and of the ordinary working of cause and effect, protests
against the compulsory registration of tuberculosis. He points
out in a philosophical and convincing way that registration cannot
be enforced, and that the attempt to enforce it will lead to decep-
tion by physicians, and that a great evil that will ensue will be
cruelty to the unfortunates who are sick with consumption. If
time permitted I could tell many tales proving the correctness of
the prediction of the bad effects of the attempts being made to
enforce registration, and of many hardships borne by consump-

tives and their friends on account of the exaggerated fear of contagion that has been fostered in the community. In contrast with this consider the statement of the governmental official written fourteen years later, and when the law for compulsory registration had been some years in effect. In language such as is ordinarily used for the description of battles he announces the failure of the law. For it is certain that it has failed if only one case in ten of tuberculosis is reported. This language of battle is inexpressibly sad. To compare military dress parades with the efforts of physicians, who can only work successfully through the channels of humanity, and who may hope by teaching prevention and hygiene and simple and easily comprehensible methods of treatment to reduce the ravages of consumption, is so unfitting that language fails to characterize it.

Statistics are often quoted, and many who have studied the records have declared that the figures prove a wonderful reduction in mortality from the disease since it has been pronounced contagious and its registration made compulsory. It has been authoritatively claimed that the "crusade against the great white plague" will in time drive consumption of the lungs from the world as a cause of death if only the enthusiasm of communities can be sufficiently aroused and great sums of money obtained to carry on the so-called crusade. No consideration is given to the fact that conclusions drawn from statistics are very difficult to make absolutely correct. Arithmetical calculations when carefully made by competent persons are absolute in their accuracy. This fact is always brought to the front by persons trying to use statistics, but the corresponding one that conclusions drawn from calculations based upon false data produce a multiplied error is generally kept in the background. The claims that have been made that the death rate has been diminished since tuberculosis has been declared to be contagious and its registration made compulsory are so extravagant that they tend to cast doubt upon all of the assertions of those who make them.

The treatment of the consumptive is better that it used to be. More effort is made, more is known of the disease, and mankind is becoming more hopeful. On the other hand, it cannot justly be said that everything is known of the effects of the outdoor life.

Outdoor treatment is often overdone for the class of people by
nature delicate and susceptible to the evil effects of cold. In the
later stages of the disease persons are sometimes exposed in cold
climates in a way that can be productive of nothing but harm.
The treatment of consumption, like the treatment of any other
disease, should be modified and adapted to the peculiarities of
each individual, and the exercise of common sense only can lead
to the best results.

If I should close my essay upon consumption of the lungs with-
out expressing any opinion upon the causation of the disease by the
bacillus of Koch, I should fail to be true to my principles. It is my
belief that the proof is still wanting that this microörganism is the
one and only cause of the disease. At the same time it goes with-
out saying that the bacillus is in the very great majority of cases
present in the tissues of those affected. There is much risk of false
conclusions being reached when deductions in regard to disease in
man are drawn from experimentation upon the lower animals.
As there have been very few injection experiments made upon
human beings, my conclusion is one which I think cannot be logi-
cally demonstrated to be false. My reasons for this conclusion
are somewhat fully set forth in my book upon *The Origin of
Disease*,[1] and from that conclusion I have not seen any good cause
to depart since the time it was originally reached.

It is becoming, in conclusion, that I should express my firm
conviction that a great deal has been accomplished to decrease the
ravages of consumption of the lungs. This, however, has been
the result of the improvement of hygienic conditions and the
attainment of a better style of living by all classes of people in
every part of the world where civilization has advanced. It is
my belief that this tendency to amelioration is like all the great
forces of Nature in that nothing can stop its progress.

DISCUSSION.

DR. LAWRENCE F. FLICK: There are a great many things in what
the essayist has said which I am sure we will all approve, namely, that
there has been too exaggerated an idea of the contagiousness of con-

[1] J. B. Lippincott Company, Philadelphia and London, 1897 and 1899, pp. 22 to 30.

sumption, and that this exaggeration has done a great deal of harm. I question, however, whether many of us can go as far as he goes, and say that the idea of the contagiousness of this disease should not be promulgated, and that harm necessarily comes from this promulgation. I do not believe that those who have advocated the contagious theory of tuberculosis have taken quite the position which he accredits to them. We have never held that tuberculosis is contagious in the sense of small-pox, measles, and those diseases. Tuberculosis is contagious in a way peculiar to itself, but scientifically we may not use any other expression than "contagious," because of all the diseases which are conveyed by a microörganism this perhaps more than any other depends absolutely for its implantation in another person upon contact; and it is because it depends so absolutely upon contact that it is not intensely contagious. This may look like a paradox, and yet it is the truth. In other words, because the microörganism of tuberculosis is given off in the way in which it is—through the sputum, or through broken-down tissue—it can easily be controlled, and in its very nature it is necessary for a person to come into contact with the disease in order to get it. You may get some of the exanthematous diseases by momentary contact because the germs which produce these diseases are given off quickly and in very large amount. But in tuberculosis it is necessary to live intimately for a long period of time in contact with the person who gives off the microörganism, or in the place in which he has given it off in sufficient amount and for a long enough time to practically infect the habitation. Now, I think this will explain the difference between the essayist's views and our views about the contagiousness of tuberculosis. We agree with him that the disease is not intensely contagious in the sense of other contagious diseases. We agree with him that it requires extraordinary exposure and intimate exposure for a long period of time, either with the individual or in the place inhabited; but we hold that no one can get tuberculosis except either by coming in contact with a person who has it, or by living for a considerable time in the place which he has infected. It is probably impossible to avoid damage from the promulgation of a new doctrine which is difficult to understand; but I think I shall be able to show, in the paper which I shall present, that even with the injury which has come to mankind from this promulgation of the doctrine of contagion it has been worth while. I believe that the essayist will live to see the day when he too will agree that it has been worth while and will see that the result could only have been accomplished in that way.

THE PROGRESS IN THE TUBERCULOSIS CAMPAIGN IN PENNSYLVANIA UP TO 1911.[1]

By LAWRENCE F. FLICK, M.D.

It may be worth while to present to the medical profession a concise statement of what has been done in the crusade against tuberculosis in Pennsylvania up to the present time, together with the results which, apparently, have been obtained with a view of profiting by the past in plans for the future. While the crusade does not concern the physician alone, it depends upon him largely for the moulding of public thought in its behalf.

The campaign against tuberculosis began formally in Pennsylvania in 1892 with the organization of the Pennsylvania Society for the Prevention of Tuberculosis. Prior to that time things had been done which might have had an influence for a reduction in the death rate from tuberculosis, although they were not done specifically for that purpose. The general hospitals and almshouses all over the State had harbored and thereby isolated advanced consumptives. The Consumptive Home of the City Mission of Philadelphia had been started in 1876 and the Rush Hospital had been founded in 1890. Dr. William Webb had taught the contagiousness of tuberculosis early in the eighties and Koch's discovery of the tubercle bacillus had been promulgated in 1882. Since 1902 the Free Hospital for Poor Consumptives and White Haven Sanatorium Association has been organized, the Henry Phipps Institute has been established, the Tuberculosis Department of the city of Philadelphia has been organized, the Montefiore Home of the Jewish Hospital has been opened, Grandview Sanatorium

[1] Read April 5, 1911.

TABLE I—Population, Gross Number of Deaths, and Death Rate per 1000 Living Persons in Philadelphia.

Year	Population	Tuberculosis of lungs	Death rate
1870	674,022	2308	3.42
1880	846,980	2692	3.17
1890	1,046,964	2764	2.64
1900	1,293,697	2717	2.10
1910	1,549,008	2873	1.85

TABLE II—Population, Gross Number of Deaths, and Death Rate per 1000 Living Persons in Pennsylvania[1]

Year	Population	Tuberculosis of lungs	Death rate
1870	3,456,609	7481	2.13
1880	4,282,891	8069	1.86
1890	5,258,014	7689	1.54
1900	6,302,115	7791	1.23
1909	7,522,800	8649	1.15

[1] The statistics in this table are inclusive of Philadelphia

of Oil City has been established, the Scranton Society for the Prevention of Tuberculosis with its sanatorium at West Mountain, the Rothrock Camp at Mont Alto, the Anti-tuberculosis Society of Harrisburg, the Wyoming Valley Society for the Prevention of Tuberculosis, the Tuberculosis League of Pittsburg with its sanatorium, and many other private organizations throughout the Commonwealth have been organized and established. The Commonwealth itself opened a large sanatorium at Mont Alto in 1907 and has established dispensaries in every part of the Commonwealth. There are now in operation 14 charitable or semi-charitable institutions for the treatment of tuberculosis with a capacity of about 600 beds, 6 pay institutions for profit with a capacity of about 100 beds, and 2 public institutions with a capacity of about 1100 beds. There are 125 dispensaries in operation, most of which give free milk and eggs and free preventive measure supplies to their patients. About $6,000,000 has been expended in Pennsylvania in the interest of the crusade against tuberculosis, and of this amount a little over $2,000,000 has been expended by private corporations, nearly $3,000,000 by the Commonwealth of Pennsylvania, and about $1,000,000 by the city of Philadelphia. Nearly $4,000,000 of the entire amount has been expended since 1907. There are now about 1800 beds available in the Commonwealth for tuberculous cases.

Statistically, there has been a reduction in the death rate from tuberculosis since 1870. Unfortunately, statistics do not always tell the exact truth, and statistics upon tuberculosis are particularly liable to error on account of change in views about the disease, change in nomenclature and in non-registration areas, change in the manner of taking the statistics. In Philadelphia we have had registration of deaths upon the certificates of physicians since 1861, but in Pennsylvania outside of Philadelphia we have had registration only since 1906, except in a few towns where we have had it since 1904. Prior to these dates, the mortality statistics in the Commonwealth outside of Philadelphia were gathered by the census enumerators from relatives every tenth year.

TABLE III—Reduction in Death Rate from Tuberculosis of Lungs per 1000 Living People in Pennsylvania[1] and Philadelphia

		Death rate	Reduction	
1870 to 1880	Pennsylvania	1.86 to 1.57	0.29	15%
	Philadelphia	3.42 to 3.17	0.25	7%
1880 to 1890	Pennsylvania	1.57 to 1.17	0.40	25%
	Philadelphia	3.17 to 2.64	0.53	16%
1890 to 1900	Pennsylvania	1.17 to 1.01	0.16	13%
	Philadelphia	2.64 to 2.10	0.54	20%
1900 to 1909	Pennsylvania	1.01 to 0.97	0.04	3%
	Philadelphia	2.10 to 1.88	0.22	10%
1870 to 1890	Pennsylvania	1.86 to 1.17	0.69	37%
	Philadelphia	3.42 to 2.64	0.78	23%
1870 to 1900	Pennsylvania	1.86 to 1.01	0.85	40%
	Philadelphia	3.42 to 2.10	1.32	39%
1870 to 1909	Pennsylvania	1.86 to 0.97	0.89	48%
	Philadelphia	3.42 to 1.88	1.54	45%
1880 to 1900	Pennsylvania	1.57 to 1.01	0.56	36%
	Philadelphia	3.17 to 2.10	1.07	33%
1880 to 1909	Pennsylvania	1.57 to 0.97	0.60	38%
	Philadelphia	3.17 to 1.88	1.29	40%
1890 to 1909	Pennsylvania	1.17 to 0.97	0.20	17%
	Philadelphia	2.64 to 1.88	0.76	29%

Reduction between 1870–1909

[1] The Pennsylvania statistics in this table are exclusive of Philadelphia

TABLE IV—Reduction in Death Rate from Tuberculosis (Generally) and Tuberculosis of Lungs (Separately) in Pennsylvania and Philadelphia, Between 1906 and 1909

			Death rate per 1000 living people	Reduction	
Tuberculosis (generally)	1906 to 1907	Pennsylvania	1.26 to 1.24	0.02	1.6%
		Philadelphia	2.50 to 2.48	0.02	0.8%
	1907 to 1908	Pennsylvania	1.24 to 1.16	0.08	6.4%
		Philadelphia	2.48 to 2.33	0.15	6.0%
	1908 to 1909	Pennsylvania	1.16 to 1.14	0.02	1.7%
		Philadelphia	2.33 to 2.16	0.17	7.3%
Tuberculosis of lungs (separately)	1906 to 1907	Pennsylvania	1.08 to 1.06	0.02	1.8%
		Philadelphia	2.18 to 2.13	0.05	2.3%
	1907 to 1908	Pennsylvania	1.06 to 0.94	0.12	11.3%
		Philadelphia	2.13 to 2.02	0.11	5.1%
	1908 to 1909	Pennsylvania	0.94 to 0.97 increase	0.03	3.0% increase
		Philadelphia	2.02 to 1.88	0.14	6.9%

Change of views about tuberculosis both as to etiology and treatment has been a cause of error in mortality statistics. The acceptance of the contagion theory by the profession and the laity has left in its wake fear and prejudice which have led to suppression and substitution of nomenclatures in deaths from tuberculosis. Suppression was very easy with the census enumerators, and during the height of the propaganda of the contagion theory may have been practised sufficiently to have influenced the mortality statistics. Substitution of nomenclatures by physicians in registration areas was probably also practised extensively, but errors which occurred in this way can be analyzed and allowed for.

The change of nomenclature of the various forms of tuberculosis which has been adopted throughout the world since the discovery of the tubercle bacillus has itself led to errors in statistics. The word "tuberculosis" was not officially introduced into the nomenclature used in Pennsylvania until 1904, but began to be used unofficially before that time and undoubtedly became a source of confusion to both the laity and the medical profession. Prior to the introduction of the word "tuberculosis" into the nomenclature the word "consumption" was used to express the idea of tuberculosis of the lungs, but was likewise used by the laity for other forms of tuberculosis which were accompanied by wasting. In registration areas the errors which grew out of this change of nomenclature can be sifted out and accounted for, but in non-registration areas this cannot be done.

Change of views about the value of climate in the treatment of tuberculosis also has led to errors in the mortality statistics. Formerly, when climate was looked upon as the only means of treating tuberculosis, many persons suffering from the disease died away from home, and the number who have died away from home has gradually decreased as the views upon the value of climate in the treatment of the disease have changed in the profession. In registration areas the deaths of citizens who died away from home have not been counted at home, while in non-registration areas where the statistics were taken by the census

Table V—Population, Deaths, Death Rate, and Reduction in Death Rate in Pennsylvania and Philadelphia, from Tuberculosis and Tuberculosis of the Lungs

PENNSYLVANIA (INCLUSIVE OF PHILADELPHIA)

Year	Population	Tuberculosis	Per 1000 living people	Reduction	Tuberculosis of the lungs	Per 1000 living people	Reduction
1906	7,099,912	10,780	1.51	....	9258	1.30	....
1907	7,256,212	10,825	1.49	1.3%	9317	1.28	1.5%
1908	7,392,431	10,211	1.38	7.6%	8703	1.18	7.8%
1909	7,522,800	10,122	1.34	2.9%	8639	1.15	2.5%

PENNSYLVANIA (EXCLUSIVE OF PHILADELPHIA)

Year	Population	Tuberculosis	Per 1000 living people	Reduction	Tuberculosis of the lungs	Per 1000 living people	Reduction
1906	5,653,024	7153	1.26	....	6097	1.08	....
1907	5,784,798	7163	1.24	1.6%	6160	1.06	1.8%
1908	5,894,486	6721	1.16	6.4%	5672	0.94	11.3%
1909	5,999,324	6826	1.14	1.7%	5810	0.97	3.0% increase

PHILADELPHIA

Year	Population	Tuberculosis	Per 1000 living people	Reduction	Tuberculosis of the lungs	Per 1000 living people	Reduction
1906	1,446,888	3627	2.50	....	3161	2.18	....
1907	1,472,414	3662	2.48	0.8%	3157	2.13	2.3%
1908	1,497,945	3490	2.33	6.0%	3031	2.02	5.1%
1909	1,523,476	3296	2.16	7.3%	2889	1.88	6.9%

TABLE VI—Death Rate per 1000 Living People from Tuberculosis, in Towns of Pennsylvania, in Two-year Periods

Town	1906–1907	1908–1909
Beaver Falls, Decrease, 14.8%	1.75	1.49
Butler, Increase, 3%	1.63	1.68
Danville, Decrease, 34.6%	2.05	1.34
Easton, Increase, 6.4%	1.40	1.49
Nanticoke, Increase, 50%	0.41	0.66
Pottstown, Decrease, 26%	0.92	0.68
Sunbury, Decrease, 27.5%	1.27	0.92
West Chester, Increase, 26%	1.95	2.46
York, Decrease, 5.5%	1.78	1.68
Braddock, Decrease, 25.3%	1.58	1.18
Chambersburg, Increase, 2.7%	1.49	1.53
Dunmore, Decrease, 28.8%	1.04	0.74
Homestead, Decrease, 13.5%	1.77	1.53
Oil City, Decrease, 7.7%	0.77	0.71
Shamokin, Decrease, 8.7%	1.04	0.95
Titusville, Decrease, 27.6%	1.30	0.94
Wilkes-Barre, Increase, 3%	0.92	0.95
Bradford, Decrease, 20.4%	0.83	0.66
Chester, Decrease, 5.8%	1.89	1.78
Duquesne, Decrease, 21%	1.23	0.97
Lebanon, Increase, 23.5%	0.89	1.10
Phœnixville, Decrease, 45.8%	1.55	0.84
Shenandoah, Decrease, 4%	0.72	0.69
Warren, Increase, 52.5%	0.59	0.90
Wilkinsburg, Decrease, 28.6%	1.15	0.82

enumerator they probably were counted at home. This would operate for an increase in the mortality rate of registration areas, while it probably would not influence the death rate in non-registration areas up until the time when registration was adopted, and then would give an apparent decrease. There is no way of eliminating the errors which have occurred in the statistics in this way.

The mortality rate from tuberculosis cannot be studied in the Commonwealth of Pennsylvania as a whole for the reasons already given, but can be studied in Philadelphia and in Pennsylvania outside of Philadelphia. Moreover, prior to 1906 in the area outside of Philadelphia it can only be studied in tuberculosis of the lungs.

Statistically, the reduction in the death rate from tuberculosis of the lungs in Pennsylvania outside of Philadelphia was from 1.86 to 1.57 per thousand (15%) between 1870 and 1880; from 1.57 to 1.17 per thousand (25%) between 1880 and 1890; from 1.17 to 1.01 per thousand (13%) between 1890 and 1900; and from 1.01 to 0.97 per thousand (3%) between 1900 and 1909. Computing the reduction upon the mortality rate in 1870 it was 37% up to 1890; 40% up to 1900; and 48% up to 1909. Since the introduction of registration in 1906 it has been from 1.08 to 1.06 per thousand (1.8%) between 1906 and 1907; from 1.06 to 0.94 per thousand (11.3%) between 1907 and 1908; and there has been an increase from 0.94 to 0.97 per thousand (3%) between 1908 and 1909. Computing the reduction upon the mortality rate in 1906, it was 10% up to 1909.

Many of the towns of the Commonwealth have had a marked reduction since 1906, while some others have had a marked increase. In this reduction and increase some allowance must be made for the natural variation from year to year in tuberculosis in small places. It is evident, however, that the reduction throughout the Commonwealth has been rather in the towns than in the country districts. With the errors which have crept into the mortality statistics of the Commonwealth in mind, it is difficult to determine what the actual reduction in the death rate in tuberculosis in Pennsylvania outside of Philadelphia has actu-

ally been, but it is fair to assume that the 48% represents the truth at least approximately. To some extent the errors in the statistics counteract each other, and while the statistical reduction in the first half of the forty-year period is probably greater than the actual reduction, we have reason to believe that the statistical reduction in the second half is less than the actual reduction.

The reduction in the death rate from tuberculosis of the lungs in Philadelphia was from 3.42 to 3.17 per thousand (7%) between 1870 and 1880; from 3.17 to 2.64 per thousand (16%) between 1880 and 1890; from 2.64 to 2.10 per thousand (20%) between 1890 and 1900; and from 2.10 to 1.88 per thousand (10%) between 1900 and 1909. Computing the reduction upon the mortality rate in 1870, it was 23% up to 1890; 39% up to 1900; and 45% up to 1909. Since 1906 it has been from 2.18 to 2.13 per thousand (2.3%) between 1906 and 1907; from 2.13 to 2.02 per thousand (5.1%) between 1907 and 1908; and from 2.02 to 1.88 per thousand (6.9%) between 1908 and 1909. Computing the reduction upon the mortality rate of 1906, it has been 13.8% up to 1909.

In Philadelphia, on account of our more accurate statistics, we are able to eliminate many errors and to get a fair idea of what the reduction in tuberculosis has been. For this purpose I have made three tables for the forty years and for each of the six years since 1904. In the first of these tables I have put those deaths which by common consent undoubtedly have been due to tuberculosis. In the second table I have put those deaths which have been recorded under an indefinite nomenclature, but ear-marked tuberculosis. In the third table I have put those deaths which have been reported under an indefinite nomenclature which may represent tuberculosis or under a nomenclature representative of diseases which simulate tuberculosis sufficiently to serve as cloaks for the suppression of deaths from tuberculosis. The three tables have been made sufficiently comprehensive to include every death which may have occurred from tuberculosis during the forty years. I have labelled the first table "tuberculosis," the second table "probably tuberculosis," and the third table "possibly tuberculosis."

TABLE VII—Death Rate per 1000 Living People from Tuberculosis, in Towns in Pennsylvania, in Three-year Periods

Town	1904 / 1905 / 1906	1907 / 1908 / 1909
Allentown, Decrease, 34%	1.93	1.27
Carlisle, Increase, 21%	1.51	1.84
Erie, Decrease, 17%	1.32	1.09
Johnstown, Decrease, 1%	0.88	0.87
Mahanoy City, Decrease, 12.5%	0.72	0.63
Altoona, Decrease, 30.7%	1.30	0.90
Columbia, Increase, 8.9%	0.78	0.85
Harrisburg, Decrease, 17%	1.35	1.12
Lancaster, Decrease, 28.4%	1.72	1.23
Meadville, Increase, 31.8%	0.88	1.16
Carbondale, Increase, 5.2%	0.95	1.00
Dubois, Increase, 36.9%	0.57	0.78
Hazleton, Decrease, 7.9%	0.88	0.81
McKeesport, Decrease, 13.7%	1.45	1.25
Mount Carmel, Decrease, 5.5%	0.70	0.66

Newcastle, Decrease, 1%

Years	Per 1000
1904, 1905, 1906	0.91
1907, 1908, 1909	0.90

Pittsburgh, Decrease, 22.7%

Years	Per 1000
1904, 1905, 1906	1.85
1907, 1908, 1909	1.43

Reading, Decrease, 12.8%

Years	Per 1000
1904, 1905, 1906	1.25
1907, 1908, 1909	1.09

Steelton, Decrease, 20.7%

Years	Per 1000
1904, 1905, 1906	1.83
1907, 1908, 1909	1.45

Norristown, Increase, 7.3%

Years	Per 1000
1904, 1905, 1906	2.60
1907, 1908, 1909	2.79

Pottstown, Decrease, 4%

Years	Per 1000
1904, 1905, 1906	2.01
1907, 1908, 1909	1.06

Scranton, Increase, 8.7%

Years	Per 1000
1904, 1905, 1906	0.92
1907, 1908, 1909	1.00

Williamsport, Increase, 8.5%

Years	Per 1000
1904, 1905, 1906	1.18
1907, 1908, 1909	1.28

Philadelphia, Decrease, 7.9%

Years	Per 1000
1904, 1905, 1906	2.53
1907, 1908, 1909	2.33

Pottsville, Decrease, 7.2%

Years	Per 1000
1904, 1905, 1906	1.37
1907, 1908, 1909	1.27

South Bethlehem, Increase, 10%

Years	Per 1000
1904, 1905, 1906	1.20
1907, 1908, 1909	1.32

TABLE VIII—Death Rate in Pennsylvania, Exclusive of Philadelphia, per 1000 Living People

	1907 Total	Per 1000	1908 Total	Per 1000	Reduction per 1000
Tuberculosis	7,264	1.25	6,760	1.15	0.10 (8.0%)
Probably tuberculosis	1,119	0.19	1,142	0.19	0.00 (0 0%)
Possibly tuberculosis	31,474	5.44	29,801	5.05	0.39 (7.1%)

	1907 Total	Per 1000	1908 Total	Per 1000	Reduction per 1000
	39,857	6.89	37,703	6.39	0.50 (7.2%)

TABLE IX—Death Rate in Philadelphia per 1000 Living People

	1870 Population, 674,022	1880 Population, 846,980	1890 Population, 1,046,964	1900 Population, 1,293,697	1910 Population, 1,549,008
TUBERCULOSIS					
Consumption of bladder					
Consumption of bowels					
Consumption of kidneys					
Consumption of larynx					
Consumption of liver					
Consumption of lungs					
Consumption of stomach					
Consumption of throat					
Hectic fever		Decrease 10 years 10.4%	Decrease 10 years 16.5%	Decrease 10 years 21.2%	Decrease 10 years 0.9%
Hemorrhage of lungs					
Lupus	3 65	3.27	2.73	2.15	2.13
Scrofula				Decrease in forty years 41.6%	41.6%
Ulceration of lungs					
Tuberculosis of lungs					
Tuberculosis of larynx					
Tuberculous meningitis					
Abdominal tuberculosis					
Pott's disease					
Tuberculous abscess					
White swelling					
Tuberculosis of other organs					
General tuberculosis					
Disseminated tuberculosis					
Acute miliary tuberculosis					
PROBABLY TUBERCULOSIS					
Abscess of chest					
Abscess of hip		Decrease ten years 17%	Decrease ten years 15%	Decrease ten years 23%	Decrease ten years 42.5%
Abscess of lungs					
Abscess, iliac					
Abscess, lumbar					
Abscess, pleural					
Abscess, psoas					

8.42	4.78	6.98	3.70	3.21	5.94	2.42	4.58
			Decrease ten years 22.6%	Decrease ten years 13%		Decrease ten years 24.6%	in forty years
					Decrease	in forty years	

years	0.50	2.63
	Decrease ten years 80%	68.7%
	89%	

Asthma
Caries of hip and spine
Chlorosis and anemia
Congestion of chest
Congestion of brain
Congestion of lungs
Debility
Diseases of brain
Diseases of chest
Diseases of hip
Diseases of lungs
Dropsy of brain
Dropsy of chest
Dropsy of lungs
Effusion on brain
Effusion on chest
Effusion on lungs
Effusion on pleura
Emphysema
Emphysema of lungs
Empyema
Fever, brain
Fever, catarrhal
Fever, continued
Fistula
Gangrene of lungs
Inanition
Inflammation of brain
Inflammation of hip
Inflammation of larynx
Marasmus
Edema of lungs
Softening of lungs
Suffocative catarrh
Tabes mesenterica
Ulceration of larynx
Laryngitis
Other diseases of larynx
Other diseases of brain
Other diseases of respiratory system
Diseases of joints
Diseases of bones
Hydrocephalus

Table X—Death Rate in Philadelphia per 1000 Living People

	1870 Population, 674,022	1880 Population, 846,980	1890 Population, 1,016,964	1900 Population, 1,293,697	1910 Population, 1,549,008
TUBERCULOSIS Consumption of bladder, of bowels, of kidneys, of larynx, of liver, of lungs, of stomach, of throat; hectic fever; hemorrhage of lungs; lupus; scrofula; ulceration of lungs; tuberculosis of the lungs, of the larynx; tuberculous meningitis; abdominal tuberculosis; Pott's disease; tuberculous abscess; white swelling; tuberculosis of other organs; general tuberculosis; disseminated tuberculosis; acute miliary tuberculosis	3.65	Decrease ten years 10.4% 3.27	Decrease ten years 16.5% 2.73	Decrease ten years 21.2% 2.15	Decrease ten years 0.9% 2.13
				Decrease in forty years 41.6%	
PROBABLY TUBERCULOSIS Abscess of chest, of hip, of lungs, and iliac, lumbar, pleural, psoas; asthma; caries of hip and spine; chlorosis and anemia; congestion of chest, of brain, of lungs; debility; diseases of brain, of chest, of hip, of lungs; dropsy of brain, of chest, of lungs; effusion on brain, on chest, on lungs, on pleura; emphysema of lungs; empyema; fever; brain, catarrhal, continued; fistula; gangrene of lungs; inanition; inflammation of brain, of hip, of larynx; marasmus; edema of lungs; softening of lungs; suffocative catarrh; tabes mesenterica; ulceration of larynx; laryngitis; other diseases of larynx, of brain, of respiratory system; diseases of joints, of bones; hydrocephalus	4.78	Decrease ten years 22.6% 3.70	Decrease ten years 13% 3.21	Decrease ten years 24.6% 2.42	Decrease ten years 80% 0.50
				Decrease in forty years 89%	
		Decrease ten years 13% 12.73	Decrease ten years 0.6% 12.65	Decrease ten years 18% 10.38	Decrease ten years 30% 7.23
	14.68				

				Decrease in forty years	50.7%
POSSIBLY TUBERCULOSIS		Decrease ten years 8%	Increase ten years 16.5%	Decrease ten years 13.4%	Decrease ten years 20.7%
Abscess of breast, of stomach; cachexia; cerebrospinal meningitis; cholera infantum; congestion of bowels, of spine; congestive chills; convulsions of children; cyanosis; diarrhea (two years and over); diseases of stomach and bowels, of spine; dysentery; effusion on spine; fever: bilious, congestive, enteric, intermittent, malarial, remittent, typhoid; hemorrhage of bowels, of stomach; inflammation of bronchi, of chest, of lungs, of peritoneum, of pleura, of spine and cord, of stomach, and bowels; influenza; perforation of intestines; stricture of bowels, of esophagus, of rectum; teething; ulceration of bowels, of rectum, of stomach and bowels; whooping cough; cholera nostras; meningitis; other diseases of spinal cord; diseases of lymphatics; ulcer of stomach; hemorrhages, except of lungs; acute bronchitis; chronic bronchitis; bronchopneumonia; pneumonia; pleurisy; gastritis; other diseases of stomach, of intestines; peritonitis; congenital debility; diarrhea (under two years)	6.25	5.75	6.70	5.80	4.60
				Decrease in forty years	26%

The reduction in the mortality of the diseases in the "tuberculosis" table and in the "probably tuberculosis" table combined has been from 8.42 to 6.98 per thousand (17%) between 1870 and 1880; from 6.98 to 5.94 per thousand (15%) between 1880 and 1890; from 5.94 to 4.58 per thousand (23%) between 1890 and 1900; and from 4.58 to 2.63 per thousand (42.5%) between 1900 and 1910. Computing the reduction upon the mortality rate of 1870, it has been 17% up to 1880; 29% up to 1890; 45% up to 1900; and 68.7% up to 1910. The two tables complement each other, the reduction being greater in one when it is less in the other. The reduction in the "tuberculosis" table for the forty years was 41.6%, and in the "probably tuberculosis" table 89%, the mean being 68.7%.

The reduction in the mortality of the diseases in the three tables combined was from 14.68 to 12.73 per thousand (13%) between 1870 and 1880; from 12.73 to 12.65 per thousand (0.6%) between 1880 and 1890; from 12.65 to 10.38 per thousand (18%) between 1890 and 1900; and from 10.38 to 7.23 per thousand (30%) between 1900 and 1910. Computing the reduction upon the mortality rate of 1870, it was 13% up to 1880; 13.8% up to 1890; 29% up to 1900; and 50.7% up to 1910. The reduction in the "probably tuberculosis" table during the forty years was 26%.

The three tables giving the gross number of deaths, the mortality rates, and the reduction in Philadelphia for each year from 1904 to 1910 show how rapidly the mortality has been reduced in recent years and how the transfer of deaths from one nomenclature to the other affects the apparent results. In these tables there has been a reduction from 2.56 to 2.13 per thousand (16.8%) between 1904 and 1910, in the tuberculosis table; a reduction from 0.74 to 0.50 per thousand (37%) in the "probably tuberculosis" table during the same time; and a reduction from 5.75 to 4.60 per thousand (20%) in the "possibly tuberculosis" table for the same time. The reduction in the tuberculosis and probably tuberculosis table combined during this period has been 20%, and the reduction in the three tables combined has also been 20%.

Table XI—Death Rate in Philadelphia per 1000 Living People

TUBERCULOSIS	Last reported	First reported	1904 Population, 1,395,821	1905 Population, 1,421,352	1906 Population, 1,446,883 Decrease one year 4.7%	1907 Population, 1,472,414 Increase one year 7.7%	1908 Population, 1,497,945 Decrease one year 0.8%	1909 Population, 1,523,476 Decrease one year 6%	1910 Population, 1,549,008 Decrease one year 9.3%	Decrease one year 0.0%
Consumption of bladder	1903									
Consumption of bowels	1903									
Consumption of kidneys	1903									
Consumption of larynx	1903									
Consumption of liver	1903									
Consumption of lungs	1903									
Consumption of stomach	1903									
Consumption of throat	1903									
Hectic fever	1886		62	63	17	14	5	6		
Hemorrhage of lungs	1899		4	6	1	1	1			
Lupus	1908			6			1	6		
Scrofula	1880			2.56	2.34	2.52	2.5	2.35	2.13	2.13
Ulceration of lungs		1904								
Tuberculosis of lungs		1904	3117	2838	3161	3157	3068	2863	2873	
Tuberculosis of larynx		1904	32	42	38	42	40	48	44	
Tuberculosis meningitis		1904	189	189	227	240	228	173	183	
Abdominal tuberculosis		1904	86	124	119	160	97	73	97	
Pott's disease		1905	17	20	21	6	23	14	14	
Tuberculous abscess	1909	1904		2	6	1	3	3	4	
White swelling		1904	5	10		9	10	14	31	
Tuberculosis of other organs	1909	1904	26	10	32	17	19	22		
Venereal tuberculosis		1904	34	34	21	29	32	22	7	
Disseminated tuberculosis		1910							7	
Acute miliary tuberculosis		1910							50	
Total			3572	3338	3644	3676	3526	3238	3303	

Decrease in six years 16.8%

TABLE XII—Death Rate in Philadelphia per 1000 Living People

PROBABLY TUBERCULOSIS	Last reported	First reported	1904 Population, 1,345,821	1905 Population, 1,421,352	1906 Population, 1,446,883	1907 Population, 1,472,414	1908 Population, 1,497,945	1909 Population, 1,523,476	1910 Population, 1,549,008	
Abscess of chest	1807									
Abscess of hip	1903									
Abscess of lungs	1903									
Abscess of iliac	1891									
Abscess of lumbar	1895									
Abscess of pleural	1879									
Abscess of psoas	1903									
Asthma	1899		51	39	60	62	61	55	80	
Caries of hip and spine			66	71	82	78	60	68	86	
Chlorosis and anemia										
Congestion of chest	1881									
Congestion of brain	1901									
Congestion of lungs			391	395	300	216	210	178	162	
Debility	1905			2	Increase one year 17.7%	Decrease one year 8%	Decrease one year 12.5%	Decrease one year 4.3%	Decrease one year 7.4%	Decrease one year 19.3%
Diseases of brain	1903									
Diseases of chest	1897									
Diseases of hip	1903									
Diseases of lungs	1887									
Dropsy of brain	1903									
Dropsy of chest	1902									
Dropsy of lungs	1903									
Effusion of brain	1900			0.74	0.87	0.8	0.7	0.67	0.62	0.50
Effusion of chest	1878									
Effusion of lungs	1886									
Effusion of pleura	1887									
Emphysema			16	15	22	17	17	13	8	
Emphysema of lungs	1892									
Empyema	1895									
Fever, brain	1890									
Fever, catarrhal	1903				Decrease	in six	years	32%		
Fever, continued	1889									
Fistula	1903									
Gangrene of lungs			11	11	6	3	6	7	6	
Inanition			65	97	70	91	115	104	76	
Inflammation of brain	1903									
Inflammation of hip	1896									
Inflammation of larynx	1903									
Marasmus			297	439	392	367	333	278	179	
Edema of lungs	1861									
Softening of lungs	1879									
Suffocative catarrh	1862									
Tabes mesenterica	1903									
Ulceration of larynx	1899									
Laryngitis		1904	17	16	20	17	16	10	5	
Other diseases of larynx		1904	11	12	3	7	6	10	12	
Other diseases of brain		1904	34	63	102	99	90	128	52	
Other diseases of respiratory system		1904	9	14	9	13	10	9	29	
Diseases of joints		1904	7		2	6	3	3	5	
Diseases of bones		1904	37	37	54	33	52	51	45	
Hydrocephalus		1904	10	27	34	30	30	26	25	
Total			1022	1238	1156	1039	1009	940	770	

In 1910 the nomenclature of "acute miliary tuberculosis" was added to the tuberculosis table with 50 deaths for that year. These deaths evidentaly were taken out of the other nomenclatures, for while the "tuberculosis" table shows no reduction in the mortality for the year, the "tuberculosis" table and the "probably tuberculosis" table combined show a reduction of 19.3%.

On the face of the records, there seems to have been a reduction of 68.7%. in the mortality rate from tuberculosis in Philadelphia since 1870. While this seems very high, it has the ear-marks of truth in its progressive ratio and in its harmony with what has been done to bring it about. More than one-half of the reduction has occurred within the last decade.

A most interesting point in connection with this reduction is the evenness of the death rate during the last forty years from all other diseases than those in the three tables. The death rate exclusive of the deaths in the "tuberculosis" and the "probably tuberculosis" tables was 14.31 per thousand in 1870; 13.93 per thousand in 1880; 14.82 per thousand in 1890; 14.80 per thousand in 1900; and 13.53 per thousand in 1910. Exclusive of the deaths in the "tuberculosis," "probably tuberculosis," and "possibly tuberculosis" tables, it was 8.04 per thousand in 1870; 8.18 per thousand in 1880; 8.11 per thousand in 1890; 9 per thousand in 1900; and 8.42 per thousand in 1910. It would seem that the decrease in the death rate in Philadelphia during the last forty years has been almost entirely due to the decrease in the death rate from tuberculosis.

What lesson can we draw from the reduction in the death rate from tuberculosis in Pennsylvania when studied in connection with what has been done to bring it about? First, that reduction in the death rate from tuberculosis apparently hinges upon isolation of open, ulcerative, pulmonary tuberculosis of the lungs; second, that the campaign against tuberculosis might be a much simpler matter than we have made it.

Prior to 1890, the only thing done in Pennsylvania with a preventive value worth considering was the isolation of open ulcerative, pulmonary tuberculosis in general hospitals and in almshouses.

TABLE XIII—Death Rate in Philadelphia per 1000 Living People

POSSIBLY TUBERCULOSIS	Last reported	First reported	1904 Population, 1,395,821	1905 Population, 1,421,352	1906 Population, 1,446,883	1907 Population, 1,472,414	1908 Population, 1,497,945	1909 Population, 1,523,476	1910 Population, 1,549,008
Abscess	....	....	22	30	31	40	40	58	52
Abscess of breast	1903								
Abscess of stomach	1902								
Cachexia	1863								
Cerebrospinal meningitis	1903								
Cholera infantum	1903								
Congestion	1882								
Congestion of bowels	1899								
Congestion of spine	1895								
Congestive chills	1898								
Convulsions									
Cyanosis	 1903	....	296	194	142	107	63	77	75
Diarrhea (two years and over)	1899								
Diseases of stomach and bowels	1903	....	319	312	319	298	263	215	309
Diseases of spine		....	51	46	42	29	36	22	31
Dysentery	1871								
Effusion of spine	1899								
Fever, bilious	1887								
Fever, congestive	1861								
Fever, enteric	1903								
Fever, intermittent									
Fever, malaria	 1903	....	11	14	5	7	6	5	12
Fever, remittent									
Fever, typhoid	 1903	....	744	684	1063	890	533	331	270
Hemorrhage of bowels	1903								
Hemorrhage of stomach	1903								
Inflammation of bronchi	1903								
Inflammation of chest	1879								
					Decrease one year 9.5%	Increase one year 17.7%	Decrease one year 8.1%	Decrease one year 10.9%	Decrease one year 12.3%

Increase one year 4.8%

Decrease in six years 20%

Disease	Year							
Inflammation of lungs	1903							
Inflammation of peritoneum	1903							
Inflammation of pleura	1903							
Inflammation of spine and cord	1903							
Inflammation of stomach and bowels	1903							
Influenza	1899	102	112	183	188	77	123	108
Perforation of intestines	1902							
Stricture of bowels	1903							
Stricture of esophagus	1902							
Stricture of rectum	1903							
Teething	1903							
Ulceration of bowels	1902							
Ulceration of rectum	1903							
Ulceration of stomach and bowels	1903							
Whooping cough	1904	327	135	221	194	387	136	73
Cholera nostras	1904	13	9	17	17	23	15	13
Meningitis	1904	73	89	77	103	84	124	249
Other diseases of spinal cord	1904	97	43	61	62	61	53	34
Diseases of lymphatics	1904	9	9	5	5	5	3	4
Ulcer of stomach	1904	57	39	48	42	77	43	53
Hemorrhages, except of lungs	1904	4	11	11	13	16	11	25
Acute bronchitis	1904	416	392	374	379	452	320	298
Chronic bronchitis	1904	118	150	150	156	186	182	185
Bronchopneumonia	1904	1125	831	1048	905	1003	652	830
Pneumonia	1904	1715	1453	1604	1835	1696	1645	2140
Pleurisy	1909	128	98	96	110	84	117	91
Gastritis	1904	249	164	180	218	222	170	146
Other diseases of stomach	1904	60	114	161	167	132	48	48
Other diseases of intestines	1904		149	63	59	37	31	24
Peritonitis	1904	8	7	16	19	34	44	56
Congenital debility	1904	372	502	551	730	635	688	726
Diarrhea (under two years)	1904	2233	1671	1697	1704	2037	1705	1475
Total		7004	6686	7504	8277	8850	7390	8021
		4.60	4.39	5.01	5.62	6.12	5.20	5.75

Before the scare about tuberculosis came over the medical profession and the public, all general hospitals and nearly all almshouses harbored and thus isolated cases of open, ulcerative, pulmonary tuberculosis, especially in the terminal stages of the disease. Some of the general hospitals devoted a great many beds to this purpose, and could an inventory be taken of the number of patients who were isolated in this way in the Commonwealth it probably would be found to be quite large. The preventive influence of this isolation upon the death rate may well have been sufficient to account for the reduction in the death rate between 1870 and 1890.

About 1890, hospitals and sanatoria for the treatment of tuberculosis began to spring up, but as they came up, the beds in the general hospitals and to some extent also the beds in the almshouses were gradually withdrawn from the use of tuberculous subjects. It is very probable that during the decade between 1890 and 1900 as many beds were thus lost to the crusade against tuberculosis by the withdrawal of beds in general hospitals and almshouses as were gained in the special hospitals and sanatoria. During this decade, dispensaries also began to spring up, but we now know that the preventive value of dispensaries is exceedingly small and would in no sense equal the value of the isolating beds in the general hospitals and almshouses. By 1900, most of the beds in the general hospitals and in the almshouses had been withdrawn, but, fortunately, by that time the number of beds in special hospitals and sanatoria had considerably increased and probably was more than equal to the loss which had been sustained. At present there is an isolating capacity in Pennsylvania of over 7000 patients a year, allowing three months for each patient. With this isolating capacity we ought to be able to reduce our death rate very rapidly all over the State.

The value of isolation of ulcerative, pulmonary tuberculosis for preventive purposes has been taught us in other countries and in other times. The Kingdom of Naples over a hundred years ago nearly wiped out tuberculosis in a relatively short time by the compulsory isolation of pulmonary tuberculosis in hospitals.

TABLE XIV—Death Rate in Philadelphia per 1000 Living People

Year	Per 1000 living people
1870	14.31
1880	13.93
1890	14.82
1900	14.80
1910	13.53

Deaths from all diseases other than those from tuberculosis and probably tuberculosis

TABLE XV—Death Rate in Philadelphia per 1000 Living People

Year	Per 1000 living people
1870	8.04
1880	8.18
1890	8.11
1900	9.00
1910	8.42

Deaths from all diseases other than those from tuberculosis, probably tuberculosis, and possibly tuberculosis

England reduced its death rate from tuberculosis 75% in less than a century by isolation of ulcerative, pulmonary tuberculosis in its consumptive hospitals; and Germany, during the last thirty years, has brought about a marvellous reduction in its death rate from tuberculosis by the isolation of its tuberculous cases in hospitals and sanatoria.

That the reduction in the death rate from tuberculosis in Pennsylvania has been largely due to the isolation which has been practised would also seem to be indicated by the topographical relationship between the reduction and the isolation. The reduction has been greatest where the isolation has been greatest. Since general hospitals and almshouses have closed their doors to consumptives, vastly the greatest amount of isolation has occurred in the city of Philadelphia, and during this time the reduction in the death rate in Philadelphia has been vastly greater than in the rest of the Commonwealth. At present, Philadelphia has an isolating capacity of about two-thirds of its mortality. Unfortunately, this isolating capacity has been somewhat reduced recently by a reduction in the number of beds in the Phipps Institute.

There is a pretty unanimous opinion among the foremost workers in the crusade against tuberculosis in all parts of the world at the present time that the most efficient measure for the prevention of the disease is the isolation of advanced cases near their own homes. It has been found that these cases can be treated in any hospital with entire safety to other inmates of the hospital provided certain simple rules of cleanliness are strictly lived up to. It is now recognized that there is practically no danger of contracting tuberculosis by mere casual contact with a tuberculous subject, and that with a proper disposal of the sputum given off in tuberculosis at the time that it is given off, every tuberculous subject can be made non-contagious and be safely kept in any environment. Had we fully understood these matters in the beginning of the campaign and made proper provision for consumptives in our general hospitals and almshouses instead of closing the doors of these institutions against such patients, we might have carried

on our campaign against tuberculosis up to the present time much more efficiently and at a smaller outlay of money. The $6,000,000 which we have expended might indeed have been enough to have wiped out tuberculosis had it been used in this way instead of the manner in which we have used it.

We undoubtedly should return to the old plan of admitting tuberculous subjects into our general hospitals in special wards set aside for this purpose, and under special control. The advanced consumptive will not go far from home for treatment, but will gladly enter a hospital near his home where he can be visited by his relatives and friends. Relatives also object to their stricken ones being removed far from home during the dying period of the disease. To get the coöperation of advanced consumptives in isolation, it is therefore necessary to make provision for them near their homes, and our general hospitals undoubtedly are most conveniently located for this purpose. We cannot go back to admitting consumptives into almshouses as paupers, but every almshouse in the Commonwealth which is not near enough to a general hospital to send its tuberculous poor to such a hospital could easily make provision for the proper isolation and treatment of advanced consumptives under its management.

We are spending much money in the campaign against tuberculosis which will bring nothing in return in the way of prevention. We will have to continue to spend some money in this way because we cannot at once change our plans, but we should make every effort to turn every dollar at our command into the channel into which it will do the most good for prevention at the earliest moment possible. It is one of the privileges and responsibilities of the medical profession to guide the public aright in this matter.

DISCUSSION.

Dr. Richard H. Harte: Being a surgeon, I have some hesitancy
in speaking upon the subject which Dr. Flick has presented this evening.
I regret that, owing to the mass of figures, it has been difficult for me
to follow the tables, but those who are acquainted with the facts stated
cannot help but recognize that the amount of tuberculosis in Pennsylvania
is gradually diminishing. This, as Dr. Meigs has already stated, may
be attributed partly to better hygienic conditions and the improved
environment of many of the people thus affected.

We know, however, that in the various institutions for the treatment
of tuberculosis, patients wonderfully improve when removed from their
homes. It has been my privilege to see a great many of these cases
treated in White Haven Sanatorium, and I must say that results seem
to me very marvellous.

As Dr. Flick has pointed out, in connection with the question of con-
tagion, it is the advanced case which presents the greatest difficulty
in preventing the spread of tuberculosis, as contagion is almost in every
instance traceable to the careless handling of advanced cases; and par-
ticularly so in reference to the cases found in our so-called slums and
poor and crowded communities of our large cities. Here contagion is
bound to arise simply from contact.

If the city and State could make some provision for dealing with
all cases of advanced tuberculosis, I think the eradication of the disease
would be comparatively simple and easily handled.

Incipient cases always arouse a certain amount of sympathy among
friends, and provision can nearly always be made for having them sent
to a sanatorium, and we know that many of them are cured. But it is
the advanced case which is, so to speak, the bugbear in the whole crusade,
and if provision can be made for taking care of it, the most tedious and
baffling conditions will have been overcome.

I think we all owe Dr. Flick a great debt for the very valuable work
he is doing, not only for the direct relief to sufferers from tuberculosis,
but in arousing the public to an appreciation of the importance of cleanli-
ness, good food, and fresh air as preventives of tubercular infection.

Dr. A. P. Francine: While it is generally realized that, from the
medical aspect, the four great factors in Education and Prevention are
in the order of their probable efficiency—the hospital for advanced cases,
the dispensary, the sanatorium, and the antituberculosis society—yet
I think the crusade must be a broader and deeper one than this would
imply, if it is to be ultimately successful in making tuberculosis a reason-
ably uncommon disease. I do not believe that, even if we had complete

adequate facilities for the proper segregation and care of every case of tuberculosis, we could stamp out this disease in the sense or to the extent which Dr. Flick thinks, though, of course, its incidence would be cut down enormously. This is not meant as in any sense an argument against the proposition that we need more beds for advanced cases and increased facilities in general. But while the crusade has developed along empirical lines, as it was bound to do, and along the only lines which were possible, and the work itself is being splendidly done, yet in a sense I feel that we are working from above downward. In other words, without ceasing our efforts and development along existing lines, we must in the future carry the crusade farther and deeper, and strike more nearly at basic underlying conditions which are responsible for the continual stream of tuberculous sick. It seems to me that the solution of our problem does not lie in caring for every advanced consumptive (though that is an absolutely necessary feature), but in raising the whole standard of living among the poor.

It must come about by bettering or doing away with slum conditions and slum life, unlivable working conditions, unsanitary homes, and in the rehabilitation of families. Control and distribution of immigration must also be a part of it; prevent the horde of ignorant foreigners from crowding into the already congested poor sections of our cities; let them be sent to outlying districts and the farms.

Another very important step, now coming to be recognized and emphasized, is the proper training and supervision of the child and the development of the resistance of the race by this means. Here open-air schools for the weakling or the tuberculous, school inspection of the right sort, education of the child and through the child the parents, are the important measures.

To conclude, I feel strongly that the tuberculosis problem is fundamentally a social and economic one, and that the care of the tuberculous sick plays in the scheme of prevention a vital but supplementary role. It is this broader and deeper view, for which personally I claim no originality, that I wish to emphasize.

Dr. B. Alexander Randall: I think there is a point in controversion of what Dr. Francine has said which is worthy of consideration. I spend part of my summers in a district which lies close between Mt. Alto and the Maryland sanatorium, and that portion of the Blue Ridge is menaced by reason of the persons leaving the sanatoria not entirely cured after a term of treatment, or sent there from the cities as to a health resort. This phase of the subject is coming to those of us who live in such regions as one deserving greater attention by the city men, who are very ready to ship their patients to the country and take little heed of the propagation of tuberculosis in the communities, hitherto free, to which such

patients are sent. I could name a half-dozen cases that have been due in that region to the taking of tuberculosis cases as boarders in the houses of the people. It may be a good thing for the patient, but a pretty poor thing for the community sometimes. Those who have an interest in such communities other than as a sanatorium neighborhood have a very serious proposition before them and one which, from the medical and other standpoints, must be handled with a good deal of care. We find that there is unquestionably a growth of tuberculosis in the vicinity of the sanatoria among people who take in these half-cured cases, especially those only half-drilled in the necessity for sputum cups and other preventive measures. It is a matter which deserves to be very carefully looked after, especially as the boarding-house keepers discourage or forbid them to take due precautions—would rather have them expectorate all over porches and lawns than be seen with a sputum cup. I think that those of us who are in the city and interested in the side here presented to us must not lose sight of the possibility of tuberculosis being fostered in the country, with serious multiplication of the foci of infection.

Dr. FLICK: I appreciate, of course, the technicality of my paper and the criticism of Dr. Harte; but to present a paper of this kind in twenty minutes without being technical and which shall be comprehensive is rather difficult. Had I been able to show my lantern slides it might have been better.

Regarding the influence of the slums upon the spread of tuberculosis, undoubtedly it should be considered; but if we could isolate all the advanced, all the ulcerative pulmonary cases, tuberculosis could not spread in the slums in spite of the unsanitary conditions. This has been demonstrated at the Phipps Institute by the statistics of the first three years' work. It was found that the slums had a much larger reduction in death rate than the best districts. In other words, it is a question of taking the seed away from the place where it can be implanted. If the seed is removed, there is no possibility of the spread of the disease. I am convinced from my study—and I am glad to say that my views correspond with those of men abroad who have made a careful study of the subject—that the important thing we have to do is to isolate the advanced consumptive. If we do that, we do not need to lie awake at night worrying about anything else. That alone will in time stamp out tuberculosis.

Dr. MEIGS, closing: The questions under discussion seem to be largely matters of opinion, and discussion by me after what I have said would probably degenerate into dispute. It is therefore hardly worth while for me to add anything to what I have already said.

CINEMATOGRAPHIC DEMONSTRATION OF NORMAL GASTRIC PERISTALSIS, AND THE PART THESE WAVES PLAY IN THE DIAGNOSIS OF CARCINOMA OF THE STOMACH.[1]

By GEORGE E. PFAHLER, M.D.

THROUGH the courtesy of Prof. Rieder, and Drs. Rosenthal and Castle, of Munich,[2] I am privileged to demonstrate to you a cinematographic film made by them about two years ago, showing normal gastric peristalsis. They first made thirteen separate plates while the subject held his breath, or in about twenty-two seconds. These separate plates were then reduced to a cinematographic film, and by means of repetition gives a fair idea of the normal gastric peristalsis.

This is not true cinematographic reproduction, the rate of exposure being too slow, but these gentlemen, who are pioneers in this field, deserve great credit for the remarkable degree of uccesss already obtained. Bio-Röntgenography, as they call it, is the only method by which these movements can be demonstrated to an audience, and by which a permanent record can be made.

In this cinematographic film which I demonstrate to you, a single wave has been recorded from its origin to its termination at the pylorus. Cole has recently succeeded in producing a cinematographic effect by making a series of separate exposures and then arranging them so that a wave effect can be followed through to the pylorus without really attempting to make them in the time required for an actual wave to pass. By his courtesy, I am permitted to show you a film of probable carcinoma, which was made by him.

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[1] Read April 5, 1911
[2] Zeitschrift für Rontgenkunde und Radium Forschung, Band xii, Heft 19.

Caldwell[1] has recently shown that actual Bio-Röntgenography will be a possibility, and while the technique and apparatus is not yet perfected, he will undoubtedly be able to make ten to twenty exposures per second, which will be the time of true cinematography.

In my opinion, a careful fluoroscopic examination gives very much more information than any cinematographic reproduction, at present, can possibly give. Cinematographically one can only demonstrate, at best, a few of the cycles of waves, and usually only one, while fluoroscopically one can follow any number of waves; one can study the effect of varying degrees of pressure, varying degrees of filling, and the effect of massage or manipulation of the stomach through the abdominal wall.

At times these waves begin to pass immediately after food enters the stomach; at other times they become strong only after ten or fifteen minutes; and at others they seem to wait for an external stimulus, such as pressure of the screen, palpation by the hand, etc. These varying conditions make it almost impossible to get at the real facts in many pathological conditions, except by a rather prolonged study fluoroscopically.

We may, in the future, be able to make such studies fluoroscopically, and, at chosen intervals, make cinematographic records. Judged by anything that I have yet seen, I believe that no actual diagnostic evidence is obtained that cannot be obtained fluoroscopically.

I speak enthusiastically of fluoroscopy, realizing fully that it is a dangerous procedure, and I think it should not be used except in such conditions as demand a study of motion, or rapidly changing relations. In other words, I confine its use to the study of the stomach, bowels, heart, and diaphragm, and I always make a number of plates at intervals during my investigation.

NORMAL GASTRIC PERISTALSIS.

The normal peristalsis begins at the upper pole as a series of slight indentations, but they only become deep enough to be of

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[1] At a regular meeting of the Philadelphia Röntgen Society, March 24, 1911.

practical importance at the junction of the middle and lower third of the stomach. At this location, a slight indentation can be seen on both the lesser and the greater curvature. These move forward and increase progressively in depth as they approach the pylorus. At about three fingers' breadth from the pylorus, they reach their maximum depth and nearly bisect the stomach. This appearance led Holzknecht[1] to look upon this contraction as a special sphincter which separates the contents of the body of the stomach from what he regarded as the pyloric antrum. This view is not accepted at present, and the deep indentations are simply regarded as a part of the regular course of the peristaltic wave, there being therefore no true pyloric antrum.

The wave seen on the lesser curvature is usually deeper than the opposite side, and moves and terminates slightly in advance of the one on the greater curvature. In my experience, the waves of the normal stomach, and in some pathological conditions are deepest, are most easily seen when the stomach is only partially filled.

In the normal stomach there are usually two or three peristaltic waves visible at one time and following each other in regular succession. It requires approximately twenty-two seconds for a wave to pass from its origin to the pylorus. Each wave seems to carry a considerable portion of the stomach contents up to the pylorus, but on account of the resistance of the pylorus most of this mass is forced back through the constriction caused by the wave.

EVIDENCE OF DISEASE AS SHOWN BY DISTURBANCE IN THE GASTRIC PERISTALSIS.

In describing the evidence of disease as is shown in disturbance of the peristaltic wave, I would not be understood to mean that a diagnosis should ever be based upon this symptom alone, nor that any other evidence should be neglected. I have confined myself to this one symptom for the sake of brevity only, and to conform to the subject under study.

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[1] Die Peristaltik am Antrum Pylori des Menschen, Mitteilungen aus dem Institute für radilegische Diagnostik und Therapie, von Dr. G. Holzknecht in Wien, Band i, Heft 1.

Carcinoma naturally first suggests itself as likely to cause disturbance in the peristalsis. As is well known, the most frequent seat of carcinoma is at the pyloric end, and since the peristaltic waves are strongest at this point, any induration of the stomach wall is bound to influence this wave.

Unfortunately, most of the cases that we have an opportunity to examine are already so far advanced that the entire pyloric end is involved, and in addition is commonly adherent. This may all be true, even when no tumor is palpable.[1] In these advanced cases the peristaltic wave stops completely at the site of the tumor. One has also the obliterations of much or all of the lumen of this portion of the stomach, associated with the rather characteristic serrated margins.

At times, however, only a portion of the pyloric end is involved. In my experience, such localization more often effects the lesser curvature. When the disease is localized in one curvature, the wave can be followed to the tumor, then become obliterated, while that on the opposite side may be seen to move smoothly to the pylorus. The most characteristic evidence is obtained when the wave can be followed to the carcinoma, becomes obliterated, and then begins again on the opposite side. When only one curvature of the stomach is involved, the wave on the opposite side is apt to be deeper than normal—apparently a compensatory effect.

I believe that in cases in which the peristaltic waves are otherwise good, an induration an inch in diameter or less should be recognized, providing it occupies the lesser or greater curvature. If it occupies the posterior or anterior surface a tumor of such size would likely be overlooked. Of course the thickness through the abdomen as well as the thickness and density of the abdominal wall will influence the clearness of the picture very much.

Pyloric Stenosis. In pyloric stenosis one is apt to find the peristaltic waves unusually deep and frequent, while they last. They may then cease entirely for an indefinite period. They may at times be excited again by external manipulation of the

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[1] In a recent contribution I called attention to the means of recognizing such adhesions, so that I will not dwell upon that phase here. Read before the Medical Section of the College of Physicians, March 27, 1911.

abdomen, by mere pressure against the screen, or by deep inspiration.

Reversed peristalsis may at times be observed in cases of pyloric obstruction. Jonas[1] and Holzknecht[2] were the first to call attention to the reversed peristalsis. I have observed it in several cases. In a case examined recently, I saw three deep waves at once apparently stand still for a short time, as if hesitating, and then move in the reversed direction.

When these reversed peristaltic waves are present, they are likely to extend nearer to the upper pole than the junction of the middle and lower third of the stomach, and the direct peristaltic waves begin higher. Reversed peristalsis is characteristic of pyloric obstruction.

The study of the peristaltic wave as applied to carcinoma of the stomach cannot be dismissed without recognition of other conditions which have a similar influence.

Gastric ulcer will at times cause tetanic or spasmodic contractions which may last an indefinite time. I have observed one case in which it lasted at least an hour and produced a decided hour-glass contraction. In such cases, of course, the peristaltic wave is interrupted. I have seen these spasmodic contractions, too, in connection with movable kidney. Generally such spasmodic contractions may be seen to relax, then a complete wave will pass, to be followed again by the spasmodic contraction. Of course an indurated gastric ulcer will give the same appearance as an early carcinoma, and it is to be hoped that more of these early cases can be examined in the future. A differentiation between ulcer and early carcinoma is as superfluous as it is impossible.

Gastric adhesions, secondary to gastric or duodenal ulcers, or secondary to a cholecystitis, will also interfere with the peristaltic wave. These involve also most often the lesser curvature. They may even cause considerable distortion of the stomach. Adhesions may involve a considerable extent of the stomach wall, and may cause displacement of the stomach without interfering

[1] Deutsche med. Wochenschrift, 1906, No. 23.
[2] Radiologische Diagnostik der intra- und extra-ventricularen Tumoren, Moritz Perle, Wien, 1908.

much with the lumen, while a carcinoma of such extent will obliterate much of the lumen, and prevent complete filling by the bismuth mixture.

I must repeat that at no time would I attempt a diagnosis upon the study of this wave alone. All other x-ray and clinical evidence and the history must be given due consideration.

Gastric atony, whether associated with neurasthenia, gastroptosis, or gastrectasis secondary to pyloric obstruction may give general absence of the peristaltic wave, or one may have to excite the wave by external manipulation. In these cases, very strong waves are likely to occur at long intervals. Therefore when they can be observed they are of special diagnostic value.

I have noticed that peristaltic waves may at times be excited by giving the patient some appetizing food after the bismuth mixture.

This hasty review of the observations regarding the peristaltic wave is given because comparatively little fluoroscopic work has been done upon the stomach in America, and it may serve as a basis, at least, for corrections and additions. Fluoroscopy has very properly been regarded by us as too dangerous. I think I have eliminated the danger from direct radiation, but not the danger from secondary rays. We are only beginning to realize the importance of these secondary rays from the air and objects in the neighborhood of an excited tube, and later we may learn that they, too, are dangerous.

CONCLUSIONS. 1. Cinematographic reproduction of the peristaltic wave of the stomach is at present possible by reducing and repeating separate exposures at comparatively long intervals.

2. Bio-Röntgenography is at present of great value in demonstrating to an audience both normal and pathological movements of the stomach.

3. In the near future we may hope to record cinematographically (10 or more exposures per second) special phases during the study of a stomach upon the fluorescent screen. This may then make it of additional value in diagnosis, since the photographic plate is more sensitive than the eye.

4. A careful study of the peristaltic wave will give the earliest evidence obtainable of carcinoma of the stomach.

DISCUSSION.

DR. JAMES M. ANDERS: I regret exceedingly that I did not hear Dr. Pfahler's paper. I am, however, quite conversant with his views. It should be noted that Dr. Pfahler does not base a diagnosis of cancer, or an ulcer, or of perigastric adhesions, upon the behavior of the peristaltic waves alone. He has expressed the belief to me that, when favorably situated, an induration of an inch in diameter, or even less, may be recognized by means of the x-rays, and he has also repeatedly pointed out before medical audiences that, as a rule, patients referred to him for an examination come when the condition from which they may be suffering is already too far advanced. It seems to me that this fact should be emphasized. I feel strongly, and have felt for a long while, that the general practitioner has not met his responsibility in respect to this matter. It is the plain duty, it seems to me, to refer even suspected cases of carcinoma of the stomach to the Röntgenologist at the earliest possible moment.

There can no longer be any question but that the results of an x-ray examination are of great advantage in the diagnosis of carcinoma of the stomach. On the other hand, there may still be some doubt as to whether the results of an x-ray examination can confirm our clinical diagnosis sufficiently early to permit of successful extirpation of the growth. This is the goal which physicians and surgeons are striving constantly to reach, and I venture to say that the x-rays will prove an important factor in its attainment.

The results of an x-ray examination, be it understood, are in no wise pathognomonic. In the very nature of the case they probably never will be. On the other hand, the x-rays can define accurately the outlines of the stomach wall. They can also show the "delay point" in the peristaltic wave, which Dr. Pfahler has demonstrated. This information, correlated with the history, the symptoms, and laboratory findings, however, facilitates an early recognition of gastric carcinoma. Either a small mass due to carcinoma or an induration caused by an old ulcer can be safely inferred from an x-ray examination, and I hold it to be the duty of physicians and surgeons to refer at the earliest possible moment their cases to the Röntgenologist. Much progress has been made in the technique of the x-rays in the field of the diagnosis of gastric diseases, and it is to be hoped that these cinematographic reproductions described by Dr. Pfahler will one day show advantages over the fluoroscope, which is not free from danger.

DR. WILLIAM L. RODMAN: I regret very much having been detained and thus prevented hearing Dr. Pfahler's paper. However, I am quite familiar with his work and have been helped most signally by it. I think the x-rays are particularly valuable in gastric diseases and especially accurate in locating hourglass contraction. In two or three cases Dr. Pfahler located the contraction absolutely, and the findings were confirmed at operation. In one case there was adhesion between the lesser curvature and the liver, so dense that I was compelled to resect a small piece of the liver in order to keep from tearing into the gastric cavity.

I also feel that the x-rays are of more or less value in carcinoma, and yet it seems to me that their greatest aid will be not so much in locating the tumor as in demonstrating a lessened peristaltic wave. I do not feel that the tumor is shown sufficiently well by the x-rays to encourage one doing radical surgery.

DR. JUDSON DALAND: I have been very familiar with Dr. Pfahler's work for more than four years. So far as the motion pictures are concerned, naturally they will be of value in teaching, more especially when the technique of their making has been improved.

The point which interests us most is that of diagnosis, more especially of cancer and ulcer with indurated edges. It is evident from the studies already made that this method is of help in this direction, as repeated observations show that the peristaltic wave is interrupted in cancer and ulcer, and the way in which this wave behaves gives some idea of the size of the lesion.

Another point of great importance is the extraordinary value of the fluoroscope versus motion pictures or skiagraphs. It is regrettable that the use of the fluoroscope is accompanied by danger, but this danger is diminished by taking the necessary precautions for protecting ourselves. Fluoroscopic work for accuracy in diagnosis is absolutely necessary. By this means we see not only the waves, but are able to judge of their vigor and frequency. I take it, therefore, that tonight we are particularly fortunate in being present at the first demonstration of this kind in this city. Last summer I saw such work in Munich, and expected to have had some films delivered to me. In the study of these cases by the Röntgenologist much depends upon his technique, manipulation, and experience. There are many conditions met with that simulate gastric carcinoma. This additional aid to the diagnosis of gastric ulcer, cancer, and spasm is most important.

PAPILLARY CARCINOMA OF THE BLADDER WITH METASTASIS TO THE TARSUS AND METATARSUS.[1]

By GEORGE ERETY SHOEMAKER, M.D.

As illustrating many points in the diagnosis and life history of papillary carcinoma of the bladder, an example may not be without interest. In August, 1909, Mrs. McC, aged sixty-nine years, multipara, was admitted to hospital because of hemorrhage of the bladder. Family and personal history negative. Bloody urine had been noted at intervals for four or five years, continuing a few days and then disappearing for months, until finally severe hemorrhage occurred. The hemoglobin was 60 per cent., the urine was negative for tuberculosis. There was a systolic murmur, edema was noted over the dorsum of the right foot, and a little pain was felt in passive motion of the tarsus. A small mass could be felt through the vagina, apparently in the bladder wall.

Careful cystoscopic study was made by Dr. George M. Laws and myself, with the resulting diagnosis of malignant papillary tumor of the bladder. There was a growth rising as a sessile prominence above the level of the mucous membrane and situated on the right anterolateral wall of the bladder between the sphincter and the right ureteral orifice. The mass was irregularly rounded in outline, pinkish red in color, and covered with clots of blood and flakes of pus. The size is shown in the photograph (Fig. 1) of the color sketch made by Mr. Schmidt. The left ureter opened by a large, reddened, pouting mouth, had stiffened sides, and did not fully contract between jets. Near this orifice was a minute prominence with an ulcerated tip and adherent

blood clot. At the upper part of the internal sphincter there was a tumor edge made up of fronds moving in the current. This tumor was light pink in color and was apparently benign. Further to the right were firmer, darker, irregularly elevated masses without fronds. At another examination indigocarmine (15 c.c. of a 0.4 per cent. solution) was injected intramuscularly in order to determine accurately the position of the right ureter and the probability of its being involved. It was found just under the edge of the principal growth and was enlarged, reddened, and swollen from either edema or infiltration.

Site of right ureteral orifice.
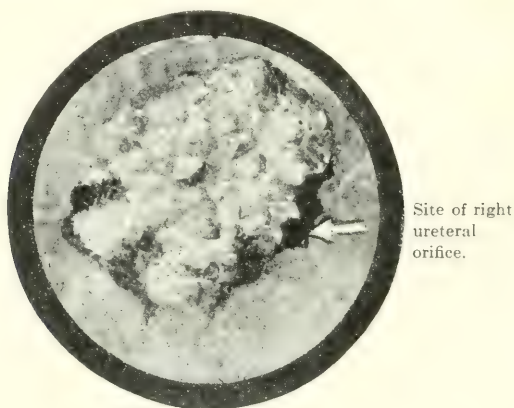
Fig. 1.—Carcinoma of bladder.

The operation of opening the bladder above the pubis was undertaken with the hope of finding the tumors observed to be capable of removal. Several distinct masses were found in the right bladder base occupying an area two or more inches in diameter. Some were of papillary form, soft and frondlike, springing from a constricted base. One of these, high on the posterolateral wall was cut away and the bleeding site controlled by purse-string suture. It proved, on microscopic examination, to be benign papilloma, and undoubtedly represented the primary growth which had been bleeding for several years. Around the internal urinary meatus were several indurations, and to the right, overlying the lower inch of the course of the ureter just as

it enters the bladder was a hard, flat carcinomatous mass, not covered by the soft fronds, but adjacent to them. Other smaller firm sessile tumors occupied a fixed portion of the wall at the base. The chief carcinomatous mass involved the right ureter. Because radical removal was not feasible the thermocautery was applied to the carcinoma and the bladder closed about a drainage tube which was conducted to a sterile urinal. This tube was finally removed on the seventeenth day and sound closure of the wound soon followed. The result of this cauterization and drainage was most satisfactory in the direction of bladder comfort and the lessening of bleeding. The nature of the disease was now clear. A benign papilloma had caused bleeding for four or five years and had probably existed for some time before it bled. A portion of it had undergone malignant degeneration, and under our observation in the hospital a secondary invasion of the right foot was at the time proceeding.

At the time of admission there was nothing about the foot to suggest a growth. There were slight varicosities of both ankles, but no bone enlargements. Three weeks later, however, pain, tenderness, and a little swelling appeared, and in two months more the condition had advanced with astonishing rapidity. A large, irregular, firm swelling involved the right tarsometatarsal articulations and near-by bony structures, especially the head of the first metartasal bone. The superficial vessels were engorged, the foot was everted below the tarsus (Fig. 2). The x-rays showed extensive disease of the bones. Under the diagnosis of secondary carcinoma amputation was advised, but first, under ether, the field was incised and frozen section made. Dr. Canby Robinson reported malignancy, and amputation was at once done through the middle third of the limb by the house surgeon, Dr. Dewitt. The object of the amputation was solely to relieve the excruciating pain in the foot which prevented sleep and exhausted the patient. The bladder symptoms were of far less moment. As a result great general improvement followed, with cessation of pain.

The tumor was examined by Dr. Speese, who has kindly furnished the following data:

The specimen consists of a foot amputated at the middle third of the tibia. About the ankle-joint there is a spindle-shaped

swelling which extends from the dorsum of the foot in the median
line to the internal malleolus. The tumor is soft in consistency, and
on incision is seen to consist of soft tissue, white in color, contain-
ing a considerable amount of necrosis. The tarsal bones are
infiltrated by the process which has resulted in the destruction of
the bone, many spicules of which appear in the tumor tissue. The
neoplasm is seen to extend along the tibia to a point about two

Fig. 2.—Metastasis of carcinoma to tarsus.

inches below the site of amputation, and to have infiltrated the
tendons of the foot to a point corresponding to the metatarsal
joint. Microscopic sections reveal a process consisting of a rather
delicate connective-tissue stroma, about the periphery of which
are arranged layers of epithelial cells, which are columnar in
shape and contain a round or rather spindle shaped nucleus.
Many mitoses are observed in these cells. Osseous tissue and in a
few places cartilaginous tissue is observed in the stroma. The

arrangement of the cells follows the type of malignancy which is seen in the papillary carcinoma of the bladder.

Pathological diagnosis: Secondary papillary carcinoma of the foot.

The relief continued for eight months, when pain recurred in the stump about two inches above the end, and a fresh metastasis appeared. The pain again became severe, and at the end of nine months the patient reappeared, imploring relief by resection of the stump. The abdominal wall had become involved, but the suprapubic incision had not opened again. To afford relief the resection was done by Dr. Ferguson, and she did well for a time, but sloughing of the abdominal wall set in, the bladder opened through the cancerous tissue, and she died exhausted between five and six years after the bleeding first appeared and about fourteen months after coming under observation. At the limited autopsy permitted, the primary carcinoma of the bladder was excised, and slides are here presented, together with others from the benign growth and from the bony metastasis.

Growths of the bladder are most frequently of the papillomatous type. They are usually benign, at least at first, and may exist for an indefinite number of years with or without bleeding or interference with function. There is a well-recognized tendency, however, for the benign to assume the malignant form, as in papillary growths of the kidney. The tendency is to slow progress and to freedom from invasion of underlying tissue. This has made their surgical removal more hopeful.

Microscopically the benign papilloma has been described as "a number of connective-tissue cores, rather rich in bloodvessels, which are covered with single or stratified polymorphous or columnar cells. If the tumor be malignant, . . . the mucosa and muscularis are found to contain masses of epithelial cells resembling those covering the papillæ of the original growth."[1] In an instance such as this of metastasis from a more central point like the bladder to a distal and remote point like the tarsus, the route by way of the lymphatic channel is out of the question. If ever a tumor cell gets into the general blood stream this would seem to be an instance of it.

[1] Adami and Nicholls, Principles of Pathology, ii, p. 781.

To explain why universal metastases are not more common from such a cause there remains the theory that on arrest or implantation of the cell some tissues afford a good soil and others do not; or that in some the local resistance is sufficient. As a matter of clinical observation these predilections have long been noted, bone metastases were found by Recklinghausen to be frequently secondary to prostatic cancer, and this has been confirmed by later experience. In all obscure carcinomas of bone an examination of the prostate gland and of the thyroid is indicated in the search for the primary lesion. The same relation to adrenal cortical tumors has been brought out by Rolleston. Leugeyer is quoted as stating that while bone metastasis occurs to the extent of 2.3 per cent. to 3.5 per cent. in uterine cancer, it follows cancer of the heart in 14 per cent. and cancer of the thyroid in 25 per cent. of instances.

The general rule that metastases follow the type of the primary lesion is well illustrated by the present case, where the occurrence of columnar types of epithelium in the bone and joint growth is contrasted with the types normally found in synovial membranes. Were there no other findings the tarsal tumor could be considered secondary from the microscopic examination.

The introduction of the tumor cell by traumatism into the blood stream is more and more the dread of surgeons. The use of the tenaculum, the curette, and the excision of portions for diagnosis of cancer of the uterus is just as dangerous without the wide use of the actual cautery as is exploratory section of cancer of the breast.

DISCUSSION.

Dr. D. B. Pfeiffer: Since Dr. Shoemaker called my attention to this very interesting case, I have taken occasion to look up the records in the laboratory of the Presbyterian Hospital.

The case illustrates to me a difficulty which I have encountered before seeing the specimens in this instance, namely, that of differentiating pathologically the benign and malignant papilloma of the bladder. That difficulty, I think, is due to the fact that benign and malignant papilloma of the bladder are probably one thing and not two things.

Both are epitheliomata, the benign form being that in which the growth is, as yet, all outward, while in the malignant form the growth has proceeded inward. Eventually this transition occurs in practically all cases.

In attempting to differentiate, therefore, we find many border-line cases in which the distinction is difficult to make. Dr. Shoemaker has already said that there is a pronounced tendency for the benign papilloma of the bladder to degenerate, as we say, into carcinoma. That is true, but it is not the entire papilloma that degenerates; not the entire growth en masse, but only a small portion. Invasion begins usually in only a single field. In examining microscopically only the projecting fronds of such a growth, I do not think that anyone can say in many instances whether the process is malignant or not. The diagnosis of malignancy depends upon the demonstration of invasion. As a precaution against missing a small amount of malignant infiltration I have made it a rule to insist that the base of the papilloma should be included with the specimen. If this is not done in a specimen such as this the diagnosis of the pathologist will not be of much use. It is essential that the base be examined and not merely the central stalk, otherwise one may easily miss the malignant infiltration.

After malignant invasion is well advanced it is often possible to give a positive diagnosis of carcinoma from the examination of a very small piece of tissue taken at random, but for a negative diagnosis to be valid the warning cannot be too strongly impressed in this type of growth, probably above all others, that a most careful search should be made of the bladder tissue upon which the growth rests before it can be considered non-invasive.

In these specimens the secondary growths were quite similar in character to the original growth, as is usually true of matastases of malignant nature. The secondary growth in the intestine, however, might easily have been mistaken for an adenocarcinoma, the cells arranging themselves in the lymphatic spaces in such a way as to suggest that a glandular lumen was present.

DR. G. M. LAWS: Examination with a Nitze cystoscope showed a growth rising as a sessile prominence above the level of the mucous membrane, and situated on the right anterolateral wall of the bladder between the sphincter and the region of the right ureteral orifice. The mass was irregularly rounded in outline, pinkish red in color, and covered with clots of blood and flakes of pus. (The size and color are shown in the sketch made by Mr. Schmidt.) The right ureteral orifice was not identified definitely, owing to the hyperemic and inflamed condition of the mucous membrane of the trigone. Its location was suggested by

jets of urine along the base of the tumor moving flakes of pus about as though they were coming from the ureter.

The left ureter opened by a large, reddened, pouting mouth, had stiffened sides, and did not fully contract between jets. Near this orifice was a minute prominence like a papule, with ulcerated tip and adherent blood clot. At the upper part of the internal sphincter there was a tumor edge made up of fronds moving in the current. This tumor was light pink in color and was apparently benign. Farther to the right side were firmer, darker, irregularly elevated masses without fronds.

At another examination indigocarmine (15 c.c. of a 0.4 per cent. solution) was injected intramuscularly in order to determine accurately the position of the right ureter and the probability of its being involved. It was then found near the base of the principal growth, and was enlarged, reddened, and swollen from either edema or infiltration.

The above findings were confirmed by Dr. Shoemaker.

FURTHER CLINICAL STUDIES IN THE AUSCULTATORY METHOD OF DETERMINING BLOOD PRESSURE.[1]

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OF PHILADELPHIA.

(From the Medical Dispensary of the University Hospital.)

In a previous paper[2] we described in full the auscultatory method of determining blood pressure, giving details of technique, with explanation of sounds heard, and calling attention to the importance of making accurate and repeated sequence readings. It may be repeated, briefly, that the method was described by Korotkow in 1906, and consists in constricting the brachial artery above the elbow in the usual manner, and then listening over the vessel at the bend of the arm. As the pressure is released a remarkable cycle will present itself. First will be heard a loud, clear-cut, snapping tone, the first phase, which is followed by a second phase, consisting of a succession of murmurs. The third phase begins with the disappearance of the murmurs and the appearance of a tone resembling in a certain degree that of the first phase, but less well marked, which soon becomes less clear in quality, or dull. At this point the fourth phase begins, and is followed by the disappearance of all sounds, the fifth phase.

In our first paper we emphasized especially the value of noting (1) tonal arrhythmias in distinguishing between functional and well

compensated cardiac diseases; (2) the absence of the fifth phase in aortic insufficiency; (3) the determining of the percentage of phase length to pulse pressure, instead of measuring in millimeters only. We suggested that more attention should be devoted to the study of the relation of individual phases one to the other, instead of laying stress on one phase alone, as other observers have done. Our clinical data was insufficient on which to base accurate conclusions concerning this point, and our object was to devote a second paper to this subject.

During the past year's study we have not found it necessary to alter the conclusions reached in our first paper, so this part may be dismissed with no further discussion. Instead, we have devoted special attention to sequence reading and to their interpretation, and it is to this aspect alone that the present paper is dedicated.

A normal cycle of auscultatory phenomena consists of five phases, the systolic pressure being 130 mm. and the diastolic 85 mm. mercury. The phases are clear-cut, and bear a definite relation to the differences between the extremes of pressure.

The phases in millimeters average as follows: First phase, 14 mm.; second phase, 20 mm.; third phase, 5 mm.; fourth phase, 6 mm. Expressing it in terms of percentage based on the pulse pressure, we find since the pulse pressure equals 45 mm. that the phases have the following percentages: First, 31.1 per cent.; second, 44.4 per cent.; third, 11.1 per cent.; fourth, 13.3 per cent., or a total of 99.9 per cent.

We interpret variations in sequence readings by assuming that each phase has a physiological factor in its production in addition to the anatomical unit, and though our hypotheses have not the firm basis of an experimental control, yet clinical experience has lent some weight to their probable correctness. Our views in this regard may be set forth as follows:

1. The first phase, or tone phase, serves principally as an index as to how far the pressure must fall before the blood current can be sustained past the obstruction in the vessel caused by the cuff, at a sufficient velocity and for a sufficient duration to produce the murmur. Hence the information it affords is of negative rather

than of positive value. In other words, its normal duration is of no value, but an increase or decrease in length is of importance.

2. The second, or the murmur phase, seems to be especially dependent upon cardiac effectiveness, for it is in this phase alone that the individual sounds possess a distinct element of duration, and this protracted energy, for so it must be regarded, must evidently come from the heart.

3. The third phase, or second tone phase, depends not alone on cardiac efficiency, but also on the character of the vessel wall. The more sclerotic the vessel and the greater the cardiac hypertrophy, the more favorable are the conditions for the production of a clear tone.

4. As the fourth phase, or dull tone, may be produced by a resilient vessel receiving a normal pulse shock, or by a rigid vessel receiving a weakened shock, its interpretation is more difficult, but its study quite as interesting.

If our assumptions as stated above are correct, then it is quite evident that increases in the second and third phases are dependent on cardiac strength and circulatory efficiency, while the first and the fourth phases suffer increase when there is cardiac weakness. Furthermore, in dealing with increases or decreases in any particular phase, it is important to know at the expense of what adjacent phase this has occurred. It is apparent that an increase in the third phase, for example, at the expense of the second, has not the same significance as an increase of this phase at the expense of the fourth. In the first instance the unit of cardiac strength, which we obtain by adding the lengths of the second and third phases, has not been materially changed, while in the latter it has been increased. For this reason, we recommend that the sum of the second and third phases be compared with the sum of the first and fourth phases, in order to determine whether the elements of force or those of weakness are predominating.

We reiterate the statement made in our previous paper, that, aside from the value of the persistence of the fourth phase in aortic insufficiency, little of diagnostic value has developed in regard to the length of any individual phase. Advantage has been derived,

however, from studying the changes in the sequence readings, especially in decompensating cardiac lesions, as the patient improves or not. In these cases changes in the percentages of the various phases are not the only significant feature, but internal peculiarities appear. Or, to put it another way, sequence readings have a functional rather than an organic significance.

Our results uniformly show that with decompensation, or circulatory disturbances of lesser degree, the element of heart weakness (the sum of the first and fourth phases) progressively encroaches upon that of heart strength (the sum of the second and third phases). The second phase appears to be the one which is with most difficulty sustained, and often the internal variations, to be spoken of later, within the element of heart strength, precede the shortening of this element as a whole. The fourth phase, as weakness gains the ascendancy, is usually the first to lengthen the element of cardiac weakness by its encroachment on the third phase, but encroachment of the first phase on the second soon adds its share to the total.

We have said that not only is the relation of the element of heart strength to that of heart weakness altered, but internal changes early appear. By internal changes we mean changes occurring in the phase itself, not as regards length, but pertaining to the relation of each individual sound to the other. Tonal arrhythmia is the most prominent of these, and simply means that there is to the ear, alternation in the intensity of individual sounds—arrhythmia of tone. We regard this form of arrhythmia as an evidence of variation in the force of individual cardiac contractions, and makes us aware of any departure from the normal before it can be discovered by palpation of the pulse or by auscultation of the heart. Tonal arrhythmias most frequently make their appearance toward the upper end of the sequence. They are first noted either as a failure of the first phase to be instituted after the first tone reaches the ear, or by a poor differentiation between the first and second phases in which tone and murmurs may alternate for a few heart beats. Internal variations in the third phase appear as the condition of cardiac weakness progresses, and are shown by alternating dull and

sharp tones or by tones of different intensity. In cases in which the arrhythmia is easily apparent to the ordinary method of examination, disturbance of auscultatory phenomena in the sequences is so pronounced as to be apparent even to a casual observer.

As a case of decompensation improves, the element of heart weakness gives place to the element of cardiac strength. The tonal arrhythmia and lack of differentiation between phases gradually disappear, commencing in the region of the third and fourth phases, and finally disappearing in the upper half of the sequence reading.

Our studies in the differentiation of cardiac neuroses from organic cardiac affections have not been met with results proportionate to the above detailed findings in other conditions, principally from a lack of material. We have had, however, a few striking cases which lead us to advance more strongly our belief that marked disparity in consecutive sequence readings, lack of uniformity in consecutive systolic and diastolic pressure estimations, when associated with internal variations in the various phases as shown by tonal arrhythmia and poor differentiation, point strongly to the presence of a cardiac neurosis when a decompensatory cardiac lesion can be excluded.

We have chosen to illustrate the above by reporting briefly our findings in two cases:

CARDIAC NEUROSES.

CASE I.—O. R., male, aged twenty years, dental student. Chief complaint, nervousness, palpitation, dyspnea, and precordial oppression, with general weakness. On examination the heat was apparently normal — no murmurs, no arrhythmia, and cardiac dulness normal. We reproduce two readings taken within a few minutes of each other.

I.				II.			
145				135			
	35.7 per cent., first phase.				44.4 per cent., first phase.		
120				115			
	14.3	"	second phase.		44.4	"	second phase.
110				95			
	50.0	"	third and fourth phases.		12.2	"	third phase.
75				90			
	Pulse pressure, 70.				Pulse pressure, 45.		

Tonal arrhythmia was marked throughout the entire sequence. Note also variations in successive systolic and diastolic pressures, and complete change in character of sequences.

CASE II.—Eliz. M., aged twenty-eight years, housewife. Chief complaint, cardiac palpitation, dyspnea, indigestion, headache, and nervousness. On examination there were no signs of cardiac weakness, no murmurs, and no arrhythmia. Successive readings on the same day:

I.			II.	
130			117	
	28.3 per cent.			27 per cent.
115			107	
	28.3 "			54 "
100			87	
	24.5 "			5 "
87			85	
	18.9 "			14 "
77			80	
Pulse pressure, 53.			Pulse pressure 37.	

Tonal arrhythmias were present, but were not so marked as in Case I. Here again are to be noted marked variations in systolic, diastolic, and in pulse pressure, also in character of sequences.

ANEMIA.

We have found the phases in anemias to be very loud and clear, and although the patient is extremely weak and relaxed, the sequence readings assume an appearance of strength. This we ascribe to the anemic condition of the blood rather than to any intrinsic cardiac efficiency.

CASE I.—Martin B., aged thirty-eight years. Diagnosis, progressive pernicious anemia. Chief complaint, weakness and shortness of breath on exertion.

118		
	22 per cent.,	first phase.
	31 "	second phase.
	33 "	third phase.
	14 "	fourth phase.
60		
	Pulse pressure, 58.	

Blood: Hemoglobin, 30 per cent.; red blood corpuscles, 1,690,000; leukocytes, 3000.

CASE II.—Margaret S., aged forty years. Diagnosis, progressive pernicious anemia. Chief complaint, edema, dyspnea, palpitation.

```
128
        18 per cent., first and second phases.
        74    "       third phase.
         8    "       fourth phase.
43
     Pulse pressure, 85.
```

There are marked tonal arrhythmias at the upper end of the sequence, the tones and murmurs alternating in such a way as to make accurate phase measurements impossible. The third and fourth phases were well differentiated and free from arrhythmias, despite edema, dyspnea, and palpitation.

Blood: Hemoglobin, 18 per cent.; red blood corpuscles, 780,000; leukocytes, 6600.

POLYCYTHEMIA.

Since in anemia the phases are loud and clear and well marked, by analogy it might be anticipated that in polycythemia the opposite should obtain. Heretofore there has been no such case studied, but through the kindness of Dr. Klaer we have had the opportunity of making blood-pressure estimations in such a condition.

William B., aged about forty-two years. Diagnosis, polycythemia.

I.	II.
128 December 23, 1910.	114 January 3, 1911.
No phases obtainable. All sounds distant and muffled.	No phases obtainable. All sounds weak and muffled.
105	93
Pulse pressure, 23.	Pulse pressure, 21.

Blood: Hemoglobin, 100 to 110 per cent.; red blood corpuscles, 8,000,000 to 11,000,000.

Our surmise was correct, for there was no differentiation of the phases possible, and the sounds had a "sticky" quality which defies description. This is the first case of polycythemia reported in literature studied with the auscultatory method of determining blood pressure, and exhibits the features which some German observers contended would accompany such a condition.

We have been interested in charting in a graphic form the blood-

pressure results obtained in various conditions. These charts are based on the percentage length of individual phases to the pulse pressure. The first one represents a normal sequence in a young subject with a healthy heart and soft arteries, and shows graphically the ratio of cardiac strength to cardiac weakness, 55.5 to 44.4. We abbreviate as follows: Cardiac strength (C. S.); cardiac weakness (C. W.).
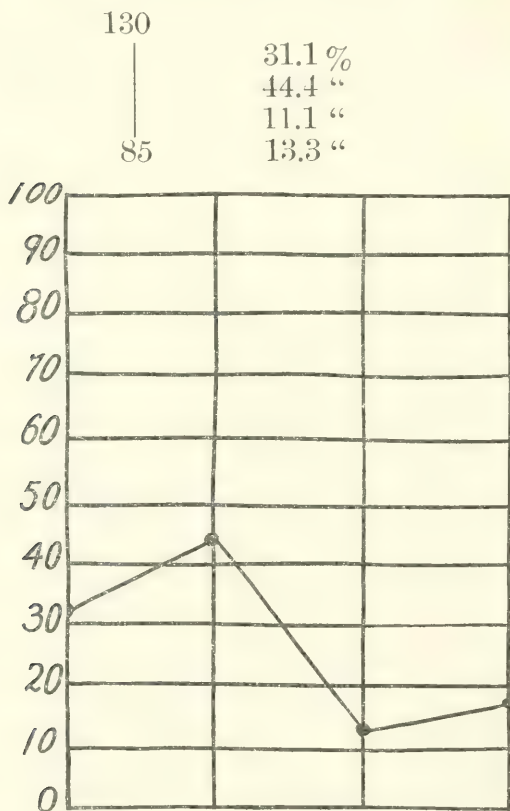
CHART I.—Normal sequence.

Considering next the pathological conditions and attempting to chart them in like form, we encountered some very interesting things.

MITRAL STENOSIS.

On admission the patient was slightly dyspneic, with duskiness of lips and hands. The chart shows graphically the elements of cardiac strength to be below those of cardiac weakness. C. S. : C. W. = 42 : 58.

115   22 %
| 20 "
| 22 "
65   36 "
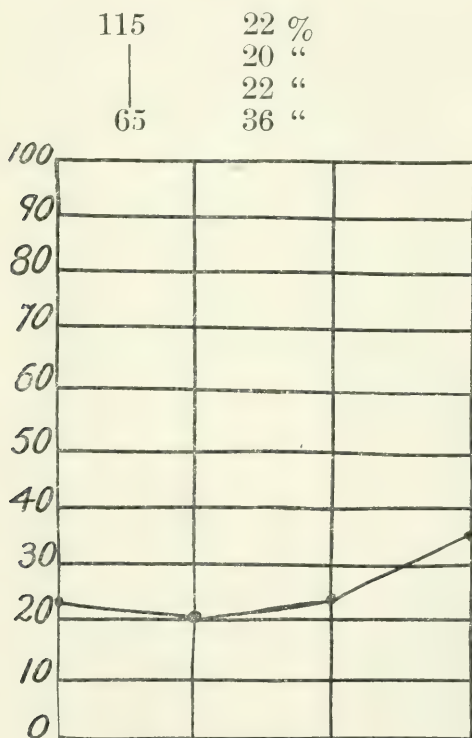
CHART II.—Mitral stenosis.

The next week on treatment there was a distinct change in the blood-pressure readings. Here in the appended Chart III is well shown the increase in the lengths of the second and third phases, with a corresponding decrease in the first and fourth. The ratio of cardiac strength to cardiac weakness is 72.5 to 27.6, and the patient was subjectively and objectively improved.

MITRAL REGURGITATION.

CASE I.—The patient, a man, aged forty-nine years, came to the dispensary complaining of cough, palpitation of heart, and dyspnea on slightest exertion. There was dilatation of the right and left
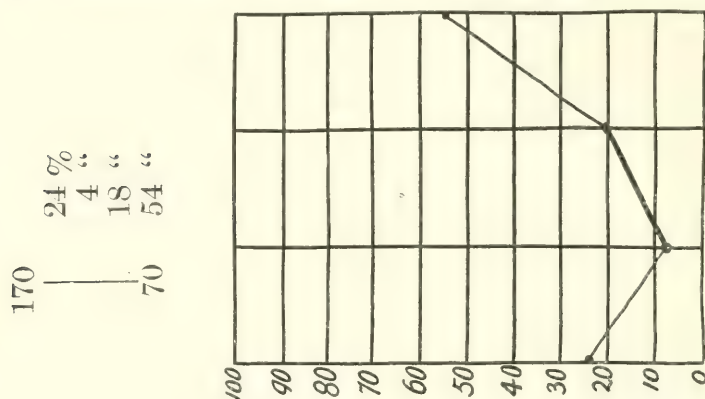
CHART IV.—Mitral regurgitation.
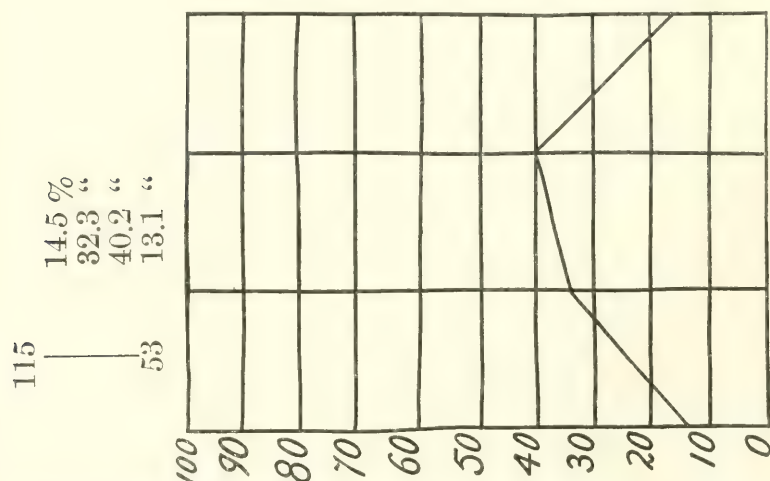
CHART III.—Mitral stenosis.

ventricle, with extrasystoles and marked arrhythmia. Tricuspid insufficiency, with pulsating liver.

There were time and tonal arrhythmias, and this factor was obtained: C. S. : C. W. = 22 : 78 (Chart IV). Later readings with improvement of the patient developed the following curve:

165   13 %
         33 "
         54 "
73   0 "
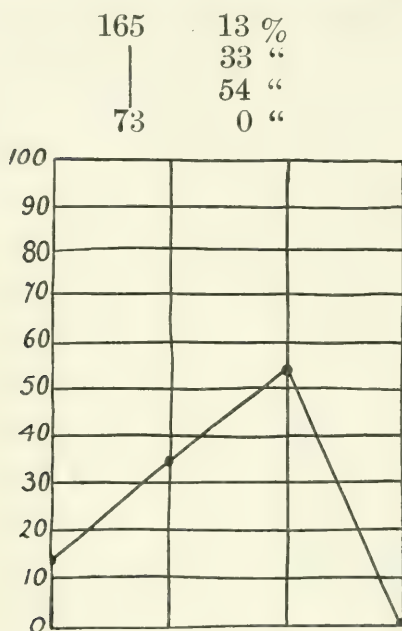
CHART V.—Mitral regurgitation.

There were no tonal arrhythmias, and C. S. : C. W. = 87 : 13. No fourth phase was obtainable.

CASE II.—On admission the patient, a man, aged eighty-three years, had failing compensation secondary to mitral insufficiency, with dilatation of right and left heart. Marked arteriosclerosis.

On admission C. S. was below C. W., there was marked tonal arrhythmia, and the phases could not be differentiated. Subjective and objective improvement were noted, and with this the two curves became divergent, the C. S. remaining above C. W.

The sequence reading is herewith appended, and bears a striking resemblance to the foregoing case, when his heart became compensated. The increase in the length of the third phase is explained by arteriosclerosis in both cases, but in Case II the arteriosclerosis was very marked. The appended chart represents the curve of the cardiac condition under treatment. The continuous lines represent the cardiac strength and the dotted lines the weakness.
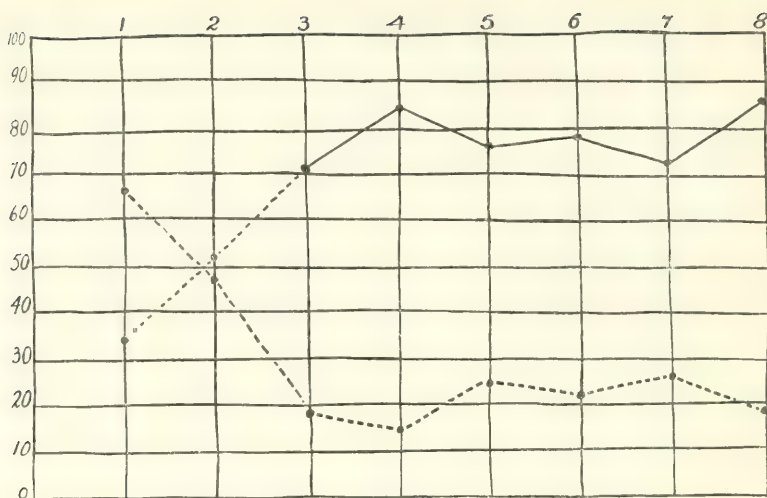
CHART VI.—Mitral regurgitation.

AORTIC INSUFFICIENCY.

On admission the blood-pressure reading was:

188
— 15 %
3 "   C. S. : C. W. = 59 : 41
56 "
0   26 "
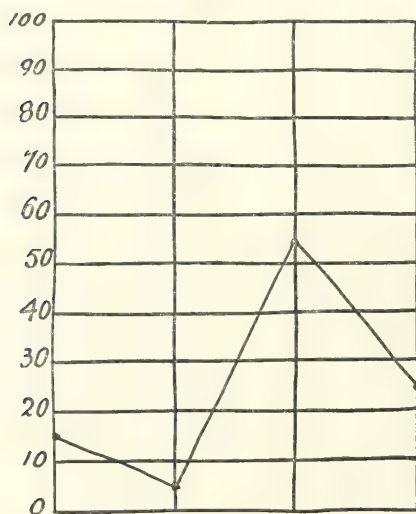
CHART VII.—Aortic regurgitation. On admission compensation poor

The pathognomonic sign of aortic insufficiency—namely, absence of fifth phase—was seen.

On account of high blood pressure, we wished to try the effect of nitrites on the circulation, with what result is graphically seen in the following chart:
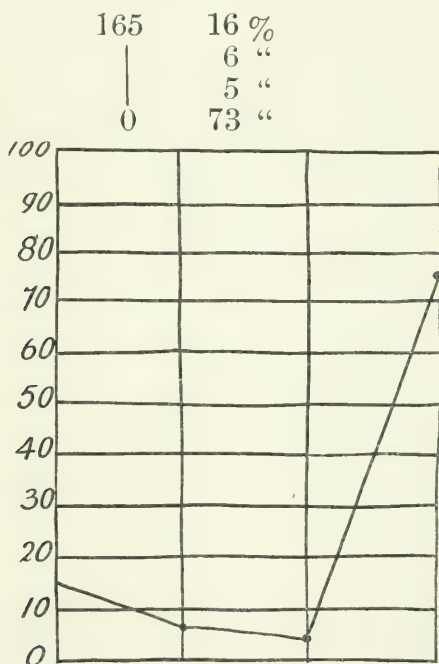
CHART VIII.—Aortic regurgitation.   Effects of nitrites prior to recuperation of heart muscle.

The blood pressure was reduced, but withal there was a falling off of C. S., so that the ratio now was C. S. : C. W. = 11 : 89.

The medication was immediately discontinued, and with fair compensation there was a return of the ascendancy of C. S. over C. W.

On this day blood pressure showed the figures represented in Chart IX.

The course of the disease is well shown by Chart X, in which we have depicted the cardiac strength (solid line) and the cardiac weakness (dotted line).
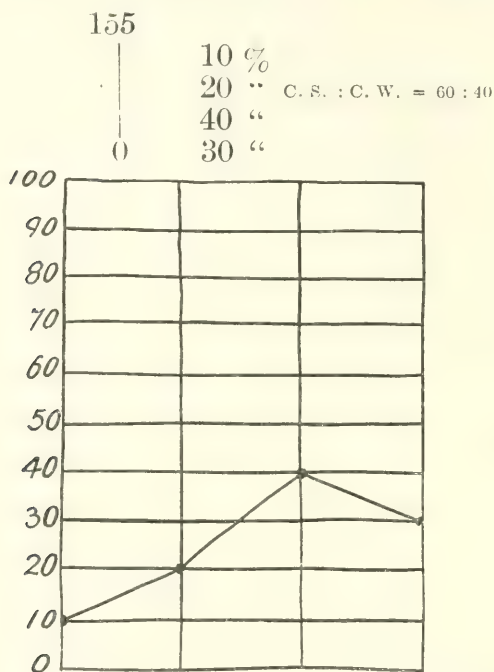
CHART IX.—Aortic regurgitation.   Compensation fair, heart muscle in better condition.
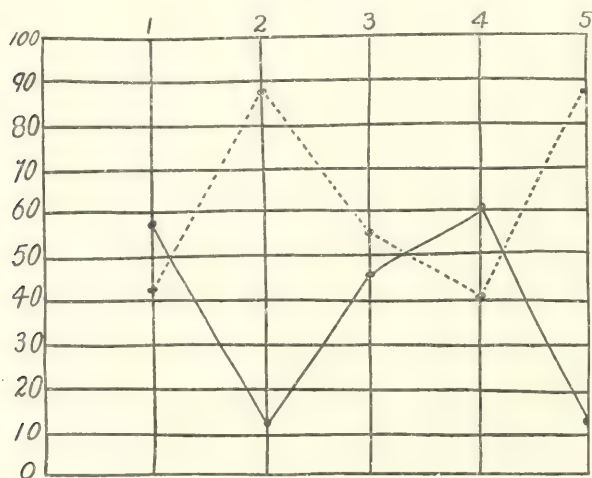
CHART X.—Aortic regurgitation.

1. On admission (Chart VII)..

2. Effect of nitrite (Chart VIII).

3. Condition of circulation improved.

4. Improvement more marked (Chart IX shows this sequence), and the patient, contrary to our advice, returned to work (ten hours on his feet as motorman).

5. As a result of the work the patient's condition became much worse, and he had to quit. The man was ill with dyspnea and marked edema, and was advised to enter the hospital. Refusing to do this, he left the dispensary and never returned.
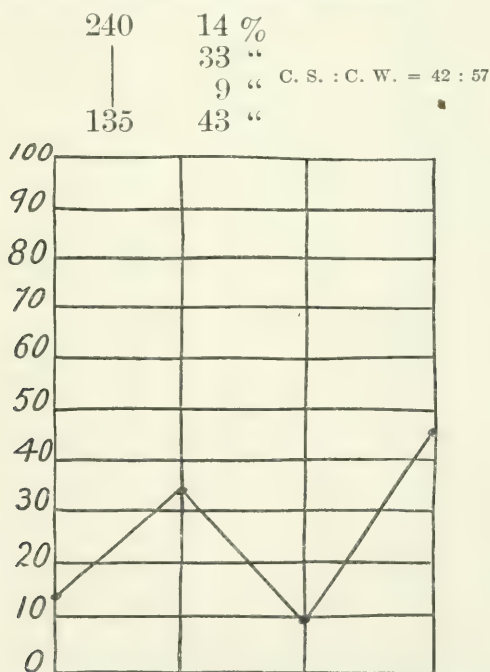
CHART XI.—Arteriosclerosis.   Uncompensated single sequence.

ARTERIOSCLEROSIS.

This patient, a man, aged sixty-eight years, was referred to us from the eye dispensary, where he had gone for dimness of vision of both eyes. There was an enormous enlargement of the heart to

the left and a moderate hypertrophy to the right. The arteries were markedly sclerosed, and later examination revealed a chronic diffuse nephritis with induration.

On admission the functional activity of the heart was not at its best, and for want of a better term we have said the heart was decompensated.

$$225 \qquad 7.3\ \%$$
$$\qquad\quad 24.2\ \text{``}$$
$$\qquad\quad 63.1\ \text{``}\quad \text{C. S. : C. W.} = 87.3 : 12.5$$
$$130 \qquad 5.2\ \text{``}$$
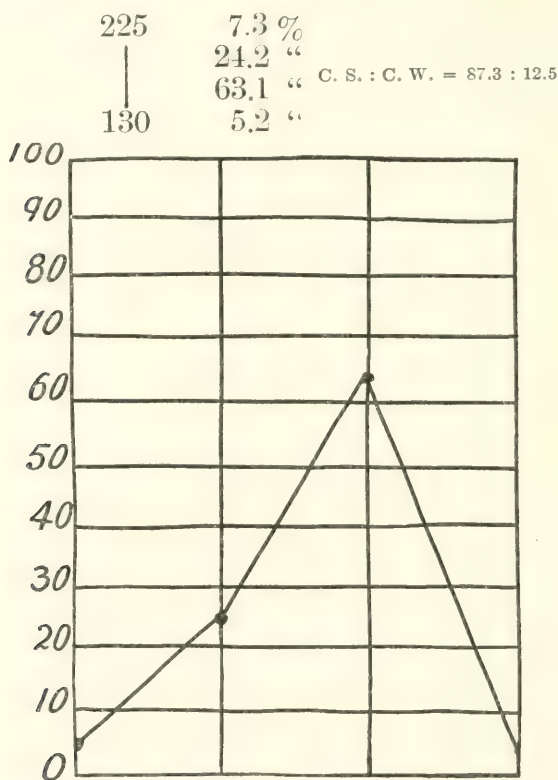
CHART XII.—Arteriosclerosis.   Compensated single sequence.

In arteriosclerosis the third phase is long, but here, owing to cardiac decompensation, it has become short (Chart XI).

When compensation set in the curve changes, and here the characteristic lengthening of the third phase is seen (Chart XII).

The course of the disease is well represented by Chart XIII.

The indication which we sought to meet was the high blood pressure, and, in addition to rest, bland diet, etc., we placed him on

large doses of sodium nitrite and nitroglycerin. The first visit
we were unable to determine his blood pressure, it being 260+.
There was a gradual fall from this figure to No. 7 (Chart XIII),
when the pressure reading was:

202
183   20 per cent.
147   38   "   C. S. : C. W. = 56 : 44.
130   18   "
108   24   "
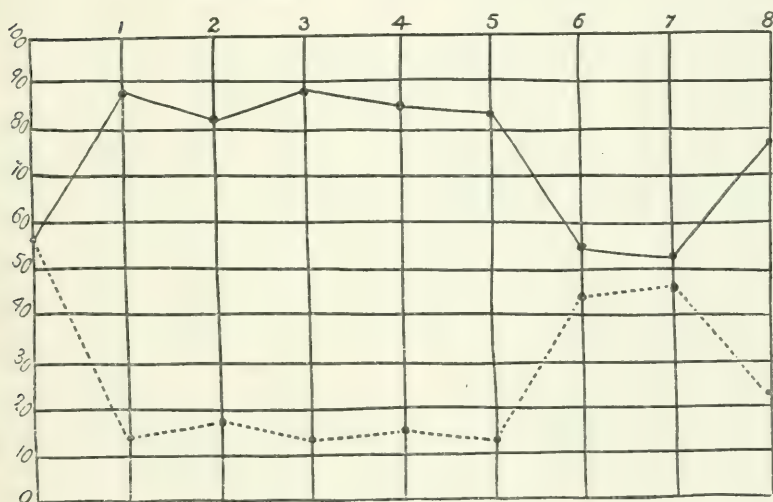
CHART XIII.—Arteriosclerosis.

On this day, as seen on Chart XIII, the two lines approximate,
and the patient felt weak, "played out," no ambition for physical
or mental effort, and the task of coming to the dispensary had
depressed him more than at any other time. The nitrites were
immediately discontinued and no medication was given, and the
next week (No. 8) the patient was improved and the blood pressure
had gone up slightly.

No. 8.
209
       17 per cent.
       28   "   C. S. : C. W. = 78 : 22.
       50   "
        5   "
116

We cannot refrain at this point from emphasizing the importance of controlling, by blood-pressure estimations, medication given to combat high pressure. In cases of hypertension the cardiovascular system has readjusted itself to altered conditions, and the normal, for them, is a pressure far exceeding the normal as given by us in Chart I. The injurious effect, or what would ultimately have been an injurious effect, is shown graphically in Charts X and XII, when, with the reduction of blood pressure, cardiac function was materially impaired.

In the case of the patient from whom Charts XI, XII, and XIII were plotted, the blood pressure was normal at about 220, or, in any case, subjectively he was best with that pressure, and with that pressure the factor was obtained of C. S. : C. W. = 87.3 : 12.5. When the pressure fell below that point the ratio of C. S. to C. W. became altered in favor of the latter, and the patient felt what is best described by the German word "Matt," and we believe he was on the verge of a vasomotor collapse, and that to have reduced the pressure still farther would have been accompanied by serious consequences. The point is not sufficiently recognized that, owing to the gradual increase of blood pressure, each individual readjusts his cardiovascular physiology to compensate this, and the physiological limit is now not 130, but may be as high as 220, as in our case. To reduce pressure below this new physiological limit is not only not indicated, but bad therapy, and hence we reiterate that with cardiac depressor drugs, or with vasodilator measures, blood pressure must be constantly watched with the sphygmomanometer.

CHRONIC NEPHRITIS.

Charts XIV, XV, and XVI represent three successive sequences taken on different days in a patient showing no circulatory symptoms. They illustrate the effect of the anemia in lengthening the second phase. We said above that arteriosclerosis was accompanied by a particularly loud, long, third phase, and it is of interest to note here

178   36 %
——   40 " "
128   10 " "
       14 "

Chart XV.—Chronic nephritis (anemia).

160   12.5 %
——   50.0 " "
120   7.5 " "
       30.0 "

Chart XIV.—Chronic nephritis (anemia).

that despite some arteriosclerosis the second phase is longer than
the third, due, we think, to the good functional state of the heart
and to the anemia.
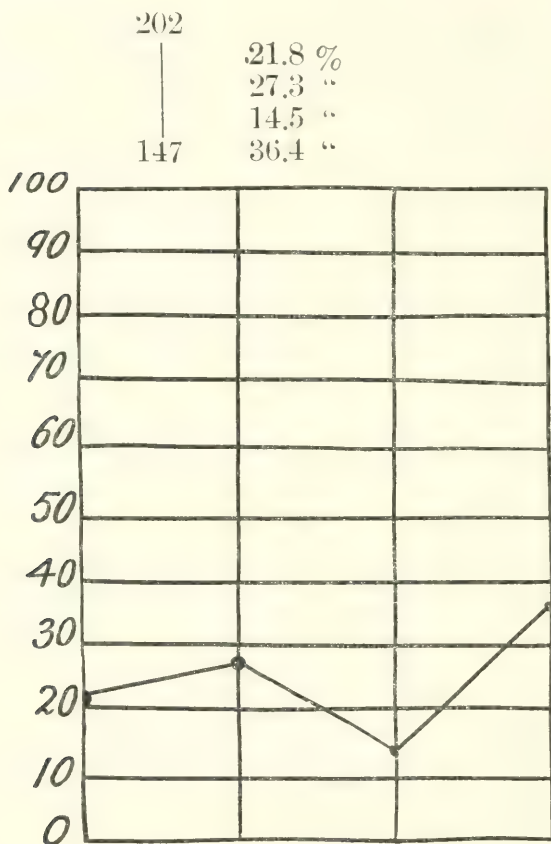
CHART XVI.—Chronic nephritis (anemia).

MYOCARDITIS.

In cases of organic disease of the heart, where the function is
impaired, as in myocarditis, the sequence readings may show no
phases, or one phase may be lacking, usually the second or third,
and with these changes tonal arrhythmias are quite easily detected.

In distinction to the functional disturbances without any apparent organic lesion, the so-called cardiac neuroses (see above), there is no variation in successive systolic and diastolic readings, which we believe to be characteristic of the neuroses.

CASE I.—Katharine D., aged fifty-five years.

> 170
> 160
>   A few murmurs alternating with tones. The tones were weak, but
>   fairly clear in quality
> 110

CASE II.—John W., aged sixty-three years.

> 157
>   No second phase.
> 90
> 85

Arrhythmia as to time, none as to intensity.

CASE III.—E., male, aged twenty-five years.

> 110
> 100   Murmurs and tones alternating. No third phase.
> 80
> 65

We feel that the auscultatory method of determining blood pressure has a large field of usefulness, and that by observing the phases and their relation to one another in each sequence reading, much may be learned of diagnostic, therapeutic, and prognostic interest.

DISCUSSION.

DR. HOBART A. HARE: I have during the last year been watching this matter of determining the blood pressure by the employment of the auscultatory method with a good deal of interest, and believe that it is a valuable addition to our means of diagnosis.

The statement made by the reader of the paper that the fifth phase does not occur in aortic regurgitation is equivalent to saying that nothing does not occur. The fifth phase is a period of silence after having been preceded by four other phases in which different sounds are heard. Instead of the sound disappearing in aortic regurgitation it persists and remains present to a point at which the pressure by the cuff seems to be almost nothing. I should like to ask the reader of the paper whether he has made any observations as to how many millimeters of mercury are

commonly present when this last phase is present, or absent as he states, in aortic regurgitation. I think I have noted it when not more than 10 millimeters of mercury are present. I think from a diagnostic standpoint the method is a valuable one to all of us. We are all inclined to the theory of aortic regurgitation as one of the most characteristic forms of valvular disease of the heart, and so it is, when well developed. On the other hand, there are cases in which the diagnosis is not so easy. Several times recently I have met with cases in which I was not able to satisfy myself that there was any capillary pulse. The feeble condition of the heart or the depth of the chest wall made it impossible to determine whether there was aortic regurgitation, but diagnosis was confirmed by the fact that the sound persisted through the fifth phase.

Another valuable diagnostic sign in my opinion, and one to which I have previously called attention, is the extraordinary variation or difference in blood pressure between the arm and the leg when the patient is reclining. There is a difference of 100 millimeters of mercury pressure between the arm and the leg in favor of the leg. If the pressure is 180 in the arm, the systolic pressure in the leg will be 280. These two comparatively new physical signs of aortic regurgitation have helped me frequently in a number of cases.

I would also like to ask the reader of the paper whether he has made any observations in regard to the influence upon these sounds in connection with pressure exercised upon the bloodvessel with the base of his stethoscope? I feel that this must cause some effect in the quality of the sounds and the persistence of these phases.

There is another point, which, while scarcely necessary to call to the attention of many, is of much importance to the general practitioner—namely, the administration of the nitrites in many cases of arterial tension with the idea that such drugs are beneficial. In fact they are often quite deleterious. Many of these cases have what might be called an abnormal norm blood pressure. I constantly see cases in which the physician having learned that 125, 135, or 140 systolic is what might be called the theoretical norm for most persons, and finding a man with a pressure of 180, gives him nitrites until he brings the pressure down to a theoretical norm, with the result that the patient may be made dangerously ill thereby.

As I understand these charts they serve to carry out the idea that many persons with high blood pressure ought not to have it reduced, or if reduced, in a very guarded fashion.

DR. GEORGE W. NORRIS: I think Dr. Goodman is to be highly congratulated upon this work which is in large measure original with him. That this new technique which he has worked out is not merely of theoretical but also of practical benefit, as is shown in the accurate way in

which the various phases fit in with different pathological conditions. Since the blood pressure has been studied by the auscultatory method almost everyone had adopted this plan to the exclusion of the older and far less satisfactory plan of oscillatory reading of the mercury. It seems to me that the adoption of this more recent method will add much to the accuracy of our observations both as to diagnosis and treatment.

I should like to emphasize what is appreciated by many and what doubtless will be appreciated by more as time goes on; the point brought out now and upon numerous occasions, by Dr. Hare; the importance of the vascular system in many diseases. It has been clearly shown that the danger of death in many diseases, such as pneumonia, lies not so much in heart failure as in failure of the vasomotor system.

DR. MAX GOEPP: I want to express my great pleasure in hearing this paper and to emphasize the importance of the point, already referred to by Dr. Hare, that every individual has a certain minimum blood pressure, and that it is not safe by artificial means to lower the pressure beyond that point. The method of studying blood pressure proposed by Dr. Goodman provides a means of determining this point of minimum pressure by instrumental observation, instead of finding out empirically by administering vasomotor depressants.

DR. GOODMAN, closing: In reply to Dr. Hare's first question, I would say that in each case of aortic insufficiency we have been able to hear either the third or fourth phase with the pressure in the cuff entirely released. In other words, the fifth phase is absent even with the manometer screw removed from the instrument.

Regarding the influence of allowing the stethoscope to press upon the artery, I would say that we do not press. What the result would be I cannot say, but I should judge it would tend to make the second phase more pronounced and perhaps increase its duration. I would caution those who use this method to exert no pressure on the artery with the stethoscope, but simply to allow it to rest thereon by its own weight.

The importance of controlling by means of blood-pressure estimations the effects of therapeutic measures levelled at the reduction of blood pressure, cannot be too strongly emphasized. As I have stated somewhat at length in our paper, each case of hypertension has, owing to the hypertension, *per se*, created for itself a new limit of blood pressure. This may be 160 mm. or it may be as high as 225 mm. as seen in one of our cases, but no reduction of blood pressure below this, *now*, for that individual, *normal* limit, is advisable, and this, what we are pleased to call normal limit, can only be determined by observing accurately subjective symptoms and the blood pressure by means of the sphygmomanometer.

The effects of nitrites in two cases can be well seen from a study of the foregoing paper.

PERFORATED ULCER OF THE STOMACH AND DUODENUM.[1]

By GEORGE G. ROSS, M.D.

WITHIN the last two years I have had four cases of perforating ulcer of the stomach or duodenum, several of which show points of marked interest in reference to the diagnosis, treatment, and end results. They are as follows:

CASE I.—Mr. Samuel M., referred by Drs. Ullom and Johnson, was admitted to the Germantown Hospital September 17, 1908. He gave a history of chronic dyspepsia, associated with vomiting and localized pain in epigastrium. He had been a sufferer from these symptoms for years. At 11 A.M. on the morning of admission he was seized with sudden, agonizing pain in the upper abdomen. The pain, which was extremely severe, radiated to the back and seemed to have its point of greatest intensity in the right iliac fossa. His abdomen was generally rigid, being most marked in the epigastric region. He was exquisitely tender over McBurney's point. There was no very great tenderness of the upper abdomen. He was operated on at 1 P.M., two hours after the onset of the attack. When the peritoneum was opened, gas and gastric contents escaped. The greatest quantity of fluid and debris was found in the right iliac fossa, although there were large quantities throughout the peritoneal cavity. A hole large enough to thrust one's thumb through was discovered in the duodenum, one-half inch from the pylorus. This was closed by through-and-through sutures and oversewn with two layers of Lembert's suture. The drainage was placed through the wound to the site of the perforation, and there was drainage through a button-hole incision above the pubes. For the first forty-eight hours after operation the patient had anuria, after which time the kidneys began to functionate. There was no evidence of either leakage or peritonitis. The material from the drains

consisted of serum, with a small amount of stomach contents. Gastro-enterostomy was not done on this patient for the reason that the anes-thetist reported the man as dead when the perforations had been closed. I believe, in view of the subsequent events, that had it been possible to have performed a gastro-enterostomy the man might have recovered.

Seven days after the primary perforation the patient had a second per-foration, with the same characteristic symptoms, resulting in death. The postmortem examination showed that there had been no leakage through the original perforation, and, while there was very little healing, the stitches had held it tight. The second perforation had occurred three-fourths of an inch from the first one, and when the duodenum was opened it was discovered that both perforations had occurred in the same ulcer, which was horseshoe-shaped, corresponding to the curve of the duodenum. There were four other ulcers of the duodenum. Dr. Ullom examined the specimen under microscope and discovered no malignant change.

CASE II.—Virgil H., aged forty years, was admitted to the German Hospital November 11, 1908; discharged January 16, 1909. The history was unfortunately overlooked, and can be remembered only in outline. The family history is unimportant. For some years the patient had been troubled with indigestion, distress after eating, and pain in the epigastrium, with eructations of gas and occasionally nausea and vomiting. He had been treated palliatively and had tried sanatorium treatment at Battle Creek, and the uses of health foods without success. Ten days before admission the patient, while walking along the street, was seized with severe pain in the hypochondrium, radiating to the back and the right chest, accompanied by nausea and vomiting, and since then he has had chills, fever, and sweats. Bowels regular. Deep breathing gave him pain in the right hypochondrium. He gradually became greatly prostrated and weak. There was a tender localized mass in the region of the gall-bladder, and a tentative diagnosis of empyema of the gall-bladder was made.

On November 12, under ether anesthesia, an incision was made through the upper right rectus. The pylorus and duodenum were found plastered tightly to the under surface of the liver, which was itself quite adherent to the abdominal wall. Upon gently releasing these adhesions, a large subphrenic abscess was encountered lying beneath the right vault of the abdomen, and a considerable quantity of yellowish, foul-smelling pus was evacuated. There was some soiling of the general peritoneal cavity. On the anterior surface of the stomach, about three inches from the pylorus, a small perforation was found, which had been closed by the adhesions which bound the stomach to the edge of the liver. The edge of the perforated ulcer was turned in by chromic gut suture and oversewn

by Lembert sutures of linen thread. The abscess cavity was drained by a rubber tube, emerging through the anterior wound, and a tube was also inserted through a counter-puncture through the right loin. Three pieces of gauze were placed about the stomach, pylorus, and subhepatic surface. Fearing soiling of the lower abdomen, a glass tube was inserted in the pelvis through a suprapubic stab. The incision was partly closed by through-and-through sutures of silkworm gut.

The patient recovered without any unusual symptoms, and upon leaving the hospital had a small discharging sinus above the pubis.

Five months after the date of operation a piece of gauze one inch wide by five inches long was passed through the suprapubic sinus, which had persisted since the removal of the glass drainage tube. It was a piece of gauze of the tube dressing which had been cut thin at one place and had become separated, and at the next dressing had been pushed through the tube and left there when the tube was withdrawn. Since this time all tubes at the German Hospital are dressed with selvage gauze.

On the day of admission the leukocyte count was 25,280, and the hemoglobin 58 per cent. The urine showed a slight trace of albumin and casts for three weeks after the operation. A culture from the pus at the time of operation showed staphylococcus.

CASE III.—Andrew B., aged fifty-five years, was admitted to the Germantown Hospital January 16, 1909; discharged January 23, 1909. The family and early personal history is of no importance. For six months prior to admission the patient had been suffering from dyspepsia. Two years ago he had a serious and severe accident, sustaining fractures of the ribs, clavicle, and right leg. At half after four o'clock on January 15, 1909, while in a barber's chair, the patient was seized by a sudden, sharp, severe pain in the upper right abdomen. He was able to walk to his home about one block away. Family remedies failing to give relief, he sent for Dr. Funk about 7.30 P.M. At this time his greatest pain and tenderness had localized in the right iliac fossa. On admission he had marked tenderness and rigidity in the right iliac fossa. Temperature, 100.2°; pulse, 100; and respirations, 32.

He was operated on at once, an incision being made through the right rectus muscle, as we believed we had an appendicular abscess to deal with. As soon as the peritoneum was incised, gas and pus escaped from the cavity. A congested appendix containing blood clots was removed. The incision was enlarged upward and plastic exudate was found under the liver and about the stomach. A perforated ulcer was found on the anterior surface of the lesser curvature of the stomach, which was closed by chromic gut suture and overwhipped by Lembert suture of silk. Cigarette and gauze drainage was inserted at the upper end of the incision, and a glass

drainage tube was inserted into the pelvic cavity. The wound was sutured between the drains. The patient apparently held his own until November 22, 1909, and then failed rapidly, and died November 23, 1909, at 6.30 P.M.

Postmortem Examination. The ulcer in the stomach which had been sutured was found healed. A perforated ulcer was found in the duodenum about 2 cm. from the pylorus. There was considerable pus in the peritoneal cavity, and the intestines were matted together by plastic exudate. An indurated and suppurating area was found in the lower lobe of the right lung.

This case illustrates several important aspects of peptic ulcer: (1) The combined peptic ulcer of the stomach and duodenum; and (2) a primary perforation of a gastric ulcer and a subsequent perforation of a duodenal ulcer. Here again the value of a gastro-enterostomy presents itself. Temporary drainage by gastro-enterostomy might have prevented the second perforation.

Case IV.—Joseph A., aged thirty-four years, born in Russia, was admitted to the German Hospital as a case of acute appendicitis with beginning peritonitis. The patient had felt well, aside from a poor appetite, until 2.30 P.M. on the day of admission. He had a piece of meat and tea for breakfast; nothing for dinner. At 2.30 P.M. he drank a glass of soda water and almost immediately was stricken with extremely severe pain across the right upper abdomen, which radiated into the right side of the back. There was some general abdominal pain, but it was most intense in the upper abdomen. He was weak and perspiring profusely. He was doubled up like a jackknife, but obtained no relief. The bowels moved well in the middle of the forenoon. No definite gastric history could be obtained. Two weeks ago the patient began to belch up a little gas, and his appetite was poor. He complained of an occasional vague pain in the epigastric region. The only noteworthy thing about this pain was that on several different occasions it was relieved by vomiting. The patient never noticed blood in the vomitus or stool. No history of gall-bladder or appendicular symptoms.

On admission, at 5.30 P.M., the patient had an anguished countenance, was restless, and complained of paroxysmal abdominal pain of severe character. Features were thin; his respiration was rapid and thoracic in type. Abdomen scaphoid, with board-like rigidity in the upper half; less marked, but present in the lower half. Extreme tenderness above umbilicus, less marked below this point. No more tenderness existed over

appendix than in corresponding point on the left side. Liver dulness extended from the sixth rib to costal margin. The flanks were clear and soft, but a tender tympanitic swelling corresponding to the size and shape of the inguinal canal was found in that area on the right side. This felt like fluid under pressure and was easily reduced, but returned immediately on the release of pressure.

An operation was performed, with the diagnosis of perforated peptic ulcer. The patient took ether badly and in large quantities. On making an incision through the right rectus, some yellow, cloudy fluid was seen, and the bowel was slightly congested and distended. The appendix was examined and found negative, but it was removed in the usual fashion, but with some difficulty, on account of the high incision. The stomach examination was negative. The duodenum was examined and a large indurated ulcer was found in the anterior surface of the duodenum about 1 cm. from the pylorus. The ulcer was about 3 cm. in diameter. In the centre of it was a small pinhead perforation through which was escaping gas and fluid. A large gray area about 1.5 cm. in diameter, surrounding the perforation, was just about ready to slough out. The whole area was turned in with silk sutures, but this was difficult on account of the poor quality of the tissue. A posterior gastro-enterostomy was done in the usual manner. A glass tube was inserted into the pelvis through a suprapubic incision, and about 50 c.c. of cloudy yellow fluid was withdrawn. The tube was removed. The neighborhood of the perforation was mopped gently, and the upper incision closed by tier sutures. The Fowler position and the Murphy treatment were employed after the operation. The further course was uneventful.

On admission the temperature was 99°, the pulse 84, and the respiration 26. A culture from the free abdominal fluid, made on November 22, was sterile. Examination of the appendix showed chronic interstitial appendicitis.

There is not any condition which the abdominal surgeon is called upon to treat in which prompt diagnosis, properly instituted treatment, and correct operative technique are more essential than in perforated ulcer of the stomach and duodenum. Ulcer of the stomach and of the duodenum can be considered together, not only because their pathology is practically identical, but also because, in view of the close relations of the two organs and their practically identical relations to other abdominal organs, the symptoms of perforation and the treatment thereof are practically the same.

THE FREQUENCY OF PERFORATION. The frequency of perforation of either gastric or duodenal ulcer is almost impossible to determine with any degree of accuracy. It has been estimated[1] that 7 per cent. of gastric ulcers will perforate. It is very doubtful if this could be verified. Clinically, the number of perforations in a series of cases of gastric ulcer not previously treated surgically, will, I believe, be found to be considerably higher.

Upon duodenal ulcer there are practically no reliable statistics as to the frequency of perforation. It should also be borne in mind that up to the last few years many ulcers which were doubtless duodenal had been classed among "gastric ulcers of the pyloric region." Thus some years ago duodenal ulcer as compared to ulcer of the stomach was considered rare; whereas now many operators, such as Mayo,[2] Moynihan,[3] and Mayo Robson, whose experience in surgery of the upper abdomen is most extensive, now regard it as being more frequent than gastric ulcer. William Mayo has called attention to a possible explanation of this. In the Mütter Lecture before the College of Physicians of Philadelphia in 1908, he drew attention to the fact that the dividing line between the stomach proper and the duodenum is indicated by a sharply defined but not generally recognized line, recognizable superficially by the course of the pyloric veins. Previously the distinction between the duodenum and the stomach had been upon general lines, and in doubtful cases the diagnosis of gastric ulcer had been preferred to that of duodenal ulcer.

It must be stated, however, that in many series of perforated ulcers of the stomach and duodenum the number of perforated gastric ulcers is so far in excess of the ulcers of the duodenum that it seems doubtful whether duodenal ulcer is really so frequent as is stated by Mayo and Mayo Robson. Thus in the experience of Miles,[4] who published the largest series of perforated ulcers of the stomach and duodenum which have occurred in any one individual practice, of 46 perforated ulcers but 10 were duodenal, while 36 were gastric. In a series of 13 cases of perforated peptic

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[1] Pariser and Linder. Quoted by Deaver and Ashhurst.
[2] Jour. Amer. Med. Assoc., 1908, p. 556.
[3] Medical Press and Circular, London, 1908, n. s., lxxxvi, 110.
[4] Edinburgh Med. Jour., 1908, n. s., xx, 106 to 117.

ulcer operated upon at the German Hospital since 1904, 10 were duodenal and 3 gastric.

LOCATION OF THE PERFORATION. The location of the perforation, both in the stomach and duodenal ulcer, is almost invariably on the anterior surface of the organ affected. Perhaps this is because the anterior surface lacks the same support that is given by the underlying structures to the posterior walls. Thus, in statistics collected by Ashhurst and Deaver,[1] 60.5 per cent. of duodenal ulcer perforations were upon the anterior wall, while the same was true of 71 + per cent. of gastric ulcers. By far the greatest number of duodenal ulcers were in the first part of the duodenum.

SYMPTOMS OF PERFORATION OF GASTRIC AND DUODENAL ULCERS. The symptoms of the perforation of an ulcer of the stomach or duodenum vary. A perforation may be either acute or rapid, chronic or slow. Rapid perforations are particularly those in which the rupture of the viscus takes place into the free abdominal cavity so suddenly that no restraining barriers of adhesions have been previously formed. Such were Cases I, II, and IV of the series which I report.

The symptoms of a rapid gastric or duodenal perforation are very similar. The first indication of perforation may come at the time of the actual perforation, although in a certain number of instances premonitory signs, such as epigastric fulness and distress, make known the fact that there is some unusual disturbance of the diseased area.

Whether or not these premonitory signs are present, the first important symptom is a sudden sharp and agonizing pain referred to the epigastrium. The patient is invariably prostrated by the pain. Moynihan mentions several instances in which patients apparently succumbed to the shock caused by the extremely severe initial pain. The pain is, as a rule, well localized to the epigastrium, but may be referred, as in Case IV of the present series, where it was referred to the right dorsal region. After a comparatively short time the most acute pain leaves the patient, but he still has a marked feeling of pain, tenderness, and heaviness

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[1] Surgery of the Upper Abdomen, 1909.

in the epigastrium. Vomiting in duodenal ulcers is so uncertain that it is not a symptom of the first importance. Hematemesis is rare in duodenal ulcers but comparatively common in gastric perforation. Elder, however, has reported a case of acute duodenal perforation in which the patient vomited bright red blood. This symptom is deceptive and hardly worthy of very great attention.

It was formerly stated that almost invariably there followed immediately with or after the pain a condition of shock. It is doubtless true that we find extreme prostration and weakness of the patient. The face is drawn and anxious, the patient perspires freely, and is somewhat pale or even slightly cyanosed in appearance. But as regards the pulse, temperature, and respiration, there is no evidence of shock until later, when a beginning septic peritonitis may give those symptoms. Thus in Case IV we find in an acute duodenal perforation, seen early, a temperature of 99° F., a pulse of 84, and respirations of 26 to the minute—certainly not significant of what is ordinarily considered as shock. The subjective symptoms, however, are not more important than those which we can discover upon thorough examination of the patient.

Abdominal palpation reveals an abdomen in which there is board-like rigidity of the recti, especially the right, and most marked in the upper abdomen. This extreme rigidity, which I have noted in my cases, is the most important diagnostic feature. The rigidity accompanying perforated ulcer in the upper abdomen far exceeds that of anything but a most unusual appendicitis or gall-bladder lesion. In association with the rigidity we find early an abdomen which may be somewhat scaphoid, but as soon as the peritoneal reaction sets in distention begins. The abdominal muscles are held rigid to protect the underlying diseased area. The diaphragm is also in close relation to the infected field, therefore we find, as we would expect, that the patient's respirations are shallow and thoracic. This is due to nature's effort to put a muscular splint upon the whole peritoneal area surrounding the acute lesion. With the marked rigidity of the upper abdomen we note a general abdominal rigidity also—and one which gradually increases as the products of peritoneal infection spread over the whole abdomen.

Tenderness in the epigastrium in cases of perforation is to be

marked early and is most severe. It has been stated that in duodenal perforation the tenderness is somewhat more to the right of the median line, while in perforations of the stomach it is to the right if the pyloric or prepyloric area be affected, and to the left if the lesion be in the body or either one of the curvatures of the viscus. The area of greatest tenderness, however, in either gastric or duodenal perforation may be about the umbilicus, and has even been referred to either iliac fossa, particularly, at times, to the right one. Leukocytosis is not always present immediately after the perforation, but appears as soon as peritonitis is in full activity. As it is an accompaniment of so many acute intra-abdominal inflammatory conditions, its usefulness is negligible and its only true value is as an indication of the patient's resistance. Moynihan and some others lay the very greatest stress upon anamnesis in the diagnosis of acute duodenal ulcer, and state that when a history of previous duodenal ulcer has not been obtained in those cases in which a perforated ulcer has been found, it is because the history has not been taken with sufficient care. In all my cases there was at least some history of gastric or digestive disturbance. Yet Elder,[1] Watson and Korte,[2] and many others mention instances in which the previous history does not point to ulcer of any sort. Korte, in a report of 18 gastric perforated ulcers and 1 duodenal perforated ulcer, says that of the 19 cases, 2 gave a history of very slight previous trouble, while 4 gave absolutely no history of disease in the upper digestive tract. We must make our diagnosis in acute perforation, then, largely upon the history of the immediate condition which causes the patient to seek treatment.

Case III of my series represents the class of subacute or slow perforations. These, as may be expected, are more common posteriorly where the adjacent viscera furnish support to the stomach and duodenum, and act as limiting structures to prevent the spread of infectious materials. In Case III, however, the ulcer was anterior. When a gastric or duodenal ulcer perforates subacutely, the symptoms are, as a rule, more protracted and less severe than in acute perforation. The course of the lesion subsequently is entirely different, for instead of the onset as a general

[1] Annals of Surgery, 1906, xliii, 390.

[2] Archiv f. Chirurgie, vol. lxxxi; Berl. klin. Woch., 1907, xliv, 226.

or diffuse peritonitis, we have the formation of a localized abscess, sometimes anterior, but usually subphrenic. The latter term as used generally will include also abscesses which have no real nearness to the diaphragm, but are merely intraperitoneal abscesses of the upper abdomen. Mayo Robson states that perforated gastric ulcer is the most frequent cause of subphrenic abscess—a statement that Deaver does not agree with, as in his experience appendicitis is the most common cause.

In addition to the general signs of perforation in such instances, we would have the local signs of a circumscribed collection, particularly if this be anterior. The whole course of the illness is less acute, and since the patient does not develop an acute and rapidly spreading peritonitis, we have the clinical picture of localized abscess, with systemic infection of the septic type. Chills, irregular fever, sweats, leukocytosis, etc.

DIFFERENTIAL DIAGNOSIS. The differential diagnosis of perforated gastric and duodenal ulcer is, as a rule, not difficult. There are, however, certain conditions which must be eliminated. Biliary colic may give pain almost as severe, and even temporary prostration as marked as that of perforated ulcer, but the subsequent hour or two with the failure of the case to show evidence of upper abdominal peritonitis will surely clear the diagnosis. Rupture of the gall-bladder is rare in the absence of definite history of previous enlargement and inflammation of the viscus. It is also absolutely far more rare than rupture of gastric or duodenal ulcer. Should it, however, occur in any instance in which the previous history did not point to a gall-bladder condition, I hardly see how it could be absolutely differentiated. In either case operation is indicated, so that the distinction is of no great importance. The conclusion that the primary pain of perforating ulcer cannot always be distinguished from that caused by disease of the biliary organs has been voiced also by Van Swerigen.[1]

The ileus may be considered to be the point of origin of the sudden severe pain. It should not, I believe, be difficult to differentiate even the most suddenly beginning intestinal obstruction from perforating ulcer. But it is interesting to note in this connec-

[1] Jour. Amer. Med. Assoc., Chicago, 1908, li, 405.

tion that in a series of 11 cases reported by Van Khnatz,[1] 2 were supposed to have had their symptoms caused by obstructions at the site of an old hernia. Probably poor history taking and rapid and superficial examination account for this error.

Menstruation is mentioned by Moynihan as having three times in his experience given symptoms which led to the diagnosis of perforated gastric ulcer. This, however, is a most unusual error in diagnosis. Perforation of malignant growth of the large and small intestines cannot, of course, be accurately diagnosticated or distinguished from other abdominal perforations unless previous history and examination point definitely to their existence.

Perforated jejunal peptic ulcer is identical in pathology and anatomy, and therefore also in symptomatology and treatment, to perforated gastric and duodenal ulcer.

Acute appendicitis is the diagnosis most frequently made where, in cases of perforated gastric and duodenal ulcer, a correct diagnosis has not been made. One of the four cases of my series was so diagnosticated before being sent into the hospital. That this is not unusual will be seen by the appended table:

Operator or reporter.	Cases of perforated ulcer.	Diagnosis of appendicitis.
Von Khnatz	11	3
Peck[2]	7	3
Federmann[3]	16 (op. 11)	2
Korte	19	2

The reason for this is twofold: (1) Acute appendicitis is the most common cause of intraperitoneal acute inflammation; and (2) perforated gastric and duodenal ulcer when discharging fluid or causing peritoneal infected fluid to form is, as a rule, so located that the fluids will gravitate toward the right iliac fossa.

Maynard Smith,[4] in a series of experiments carried out upon the cadaver, found that the fluid from such a source in a patient in a recumbent position followed the following course: (1) Downward in the direction of the right kidney pouch; thence (2) along the

[1] Archiv f. klin. Chir., 1908, lxxxv, 700 to 717.
[2] Medical Record, New York, 1907, lxxii, 930 to 934.
[3] Deutsch. Zeit. f. Chir., 1907, lxxxvii, 443 to 481.
[4] Lancet, 1906, i, 895.

outer side of the ascending colon as far as the brim of the pelvis; thence (3) overflowed into the pelvis. Hence we can see why trouble of the appendix is so closely simulated, especially as Van Sweringen points out, after the lapse of about twelve hours.

It must not be forgotten that perforated duodenal ulcer and acute perforative appendicitis may be coincident. Indeed, Graham[1] reports a case in which a perforated retrocolic appendix formed part of the wall of an abscess originating from a perforated duodenal ulcer.

Acute pancreatitis has been mistaken for a perforated gastric or duodenal ulcer. There is no doubt that the early distinction is most difficult; but, as the case progresses, there is noted the gradual toxemia of pancreatitis, the absence of the characteristic rigidity of perforation, and the evidence of an infection of the omental bursa, and the marked symptoms of high intestinal obstruction—diaphragmatic pleurisy, diaphragmatic hernia.

Richardson,[2] in a most careful article, has drawn attention to the frequency with which actue intrathoracic disease simulates the symptoms of acute intra-abdominal lesions.

Barnard[3] reports an instance in which double basal pneumonia with a right diaphragmatic pleurisy in a patient with an unperforated gastric ulcer gave rise to symptoms leading to a diagnosis of perforation.

The appendix as a cause of disease simulating upper abdominal disease has come more and more into prominence within the last few years. I have already mentioned the frequency with which acute upper abdominal disease is diagnosticated appendicitis. While the reverse condition is not so common, it must not be forgotten that appendicitis, especially of the chronic variety, often gives rise to crisis of pain referred to the upper abdomen, occasionally accompanied by hemoptysis (Fenwick).[4] The occurrence of pylorospasm as a result of chronic appendicitis is not common, but nevertheless is mentioned by several authors, among them Deaver and Ashhurst. It might even be possible that an acute fulminating attack of appendicitis might give rise to the symptoms of perforated gastric or duodenal ulcer, but we are far more likely to find

[1] Annals of Surgery, 1904, xl, 447.   [2] Boston Med. and Surg. Jour., 1902, i, 399
[3] Lancet, 1902, ii, 280.   [4] Dyspepsia, London, 1910, p. 78.

it in a confusing element in the anamnesis when attempting to elicit a history of upper abdominal disease prior to the suspected perforation.

Finally, the possibility of a diaphragmatic hernia must be considered, although this condition is practically never diagnosticated during life except by operation.

Hysteria or unperforated ulcer with peritonitis may all give rise to symptoms very closely simulating those of perforated ulcer.

The distinction between gastric and duodenal perforation is not always difficult; in fact, Moynihan considers it comparatively easy in most instances. Sometimes the anamnesis makes the case clear at once. At other times the distinction is more doubtful, because the history is less clear. In either case the practical importance of the matter is not very great because our treatment is the same for both gastric and duodenal ulcer.

TREATMENT. The treatment of perforated gastric and duodenal ulcer is in its main aspects entirely surgical. Nothing is surer than the fatal termination of a perforative peritonitis of the upper abdomen in all but the rarest instances when a surgeon is not put in charge of the case. The patient's only chance for recovery under medical treatment is in the formation of a localized abscess with spontaneous evacuation other than into the general peritoneal cavity, a termination so rare that it need not be considered.

The time of election in operation for perforated gastric and duodenal ulcer is at once when the case is seen. All statistics agree that in those instances where acute perforation takes place and the infection is not circumscribed, early operations are by far the most successful. Thus, Van Khnatz had:

	Mortality, per cent.
5 cases operated in the first twelve hours; 3 died	60
1 case operated in the first eighteen hours; 0 died	0
5 cases operated after the first two days; 5 died	100

Or,

In the first twenty-four hours, 6 operated; 3 died	50
After forty-eight hours 5 operated; 5 died	100

Martens[1] had in 11 cases 6 recoveries, all operated upon from two and one-half to twenty-six hours after perforation.

[1] Deutsche med. Woch., 1907, xxxiii, 1851.

Robson and Moynihan[1] give the following mortality in per cent. for perforated gastric ulcer: Under twelve hours, 28.5 per cent.; twelve to twenty-four hours, 63.6 per cent.; twenty-four to thirty-six hours, 87.5 per cent.; thirty-six to forty-eight hours, 100 per cent.; over forty-eight hours, 51.5 per cent. had evidently had time to localize.

Patterson,[2] in a consecutive series found in cases operated under twelve hours, 47 per cent. mortality; twenty-four hours, 50 per cent. mortality; twenty-four to forty-eight hours, 83 per cent. mortality.

There are a number of reasons why it is of the utmost importance to operate early in cases of gastric and duodenal ulcer. In the first place it is well known that in any peritonitis beginning in the upper abdomen early operation offers the patient the very best chance of recovery. Early operation avoids the absorption of toxins and anticipates the loss of the patient's vitality caused thereby. It enables us to intervene when the disease process is still localized to some extent, and has not reached the stage of general peritonitis. In cases of gastric and duodenal perforation it is even more important, however, to deal with the resultant peritonitis early than it is in inflammations of the lower abdominal or pelvic viscera. I have mentioned the path of diffusion of the toxic fluids formed or liberated within the upper right quadrant of the abdomen. There is in so many instances no attempt at localization that often we have a rapid spread of infectious material in a purely mechanical way. Naturally, if we operate in the first stage of a perforation, this mechanical diffusion will not be far advanced, and we have to deal with a more or less localized peritonitis instead of one which is diffused or general.

Moreover, it has been pointed out by Murphy[3] and others that the diaphragmatic zone of the peritoneum is by far the most absorptive area of the whole membrane. Infectious materials are absorbed with far greater rapidity by the diaphragmatic peritoneum than by any other portion, and not only is this true, but we have found that the whole upper abdominal peritoneum shares

[1] Diseases of the Stomach, 1907, p. 101.　　　[2] Lancet, 1906, i, 575.
[3] Surg., Gynec., and Obstet., Chicago, 1908, vi, 575 to 598.

to a certain extent this great power of absorption. Thus while a pelvic or lower abdominal condition, such as appendicitis or salpingo-oöphoritis, occurs in the area in which there is a certain possibility of defense against toxins, exactly the reverse is true of a perforated gastric or duodenal ulcer. On this account, again, it is most important to remove both the source of infection and the infectious material already formed at the earliest possible moment. I have no doubt that when it becomes the usual thing among medical men and surgeons accurately to diagnosticate such conditions early, and to operate at once under practically all conditions, the mortality will be reduced to a point far below that reached by any operator so far.

The operation itself must accomplish three things primarily: (1) It must include some form of closure of the ruptured ulcer; (2) it must adequately provide for the drainage, etc., necessary for the care of the peritoneal condition; and (3) under favorable circumstances, it may seek to prevent a recurrence of the perforative process. It is, of course, imperative that at the time of operation we should locate the perforation itself. After making the incision into the upper abdomen, a foul fluid, possibly containing portions of foodstuffs, may be discovered. If this be caused by a perforated ulcer of the alimentary tract, we often have also an escape of gas from the wound. Our diagnosis is then certain. Before proceeding any farther we should at least attempt to prevent further diffusion of infectious materials during the operation itself by the proper use of large gauze pads to wall off the infected area. I am certain that the proper use of such barriers to infection in all operations for localized or even diffused peritoneal infections is of the utmost importance. It should be our object to introduce at once these pads, not only so that they effectually limit the spread of pus, etc., during the operation, but also that by their rough introduction and handling they do not denude the peritoneum of its endothelial coat and thus give rise to the subsequent formations of adhesions. If the rough handling of the clean peritoneum may give rise to the postoperative adhesions, these are certainly more apt to form when infection is already present. These pads also act as a sponge while in the general peritoneum.

When the operative area has thus been limited we may proceed

in our endeavor to find and close the perforation. In cases beyond the first few hours there is often quite an amount of plastic lymph about the infected area. This should be removed only when it is in the road of the operator; otherwise it should not be disturbed, as there is reason to believe that it has a protective function. The omentum also has often come to the rescue and its adhesions should be gently separated so that we do not cause additional damage to the upper abdominal structures. Often, too, the omentum itself has covered the perforation and has acted as a temporary plug, preventing further escape of infectious material and localizing the peritonitis. By care in the use of our pads and careful though not slow operative procedures, it is often possible to complete the operation without further spreading the pus present.

When the perforation has been found there are several points which must engage the surgeon's particular attention. In the first place, it is always wise to determine whether or not the perforation is single. It is true that multiple simultaneous perforation of the stomach or duodenum is the exception rather than the rule, yet they have been reported. Secondly, we should endeavor to make sure that the ulcer is not accompanied by others not yet perforated, but about to do so. In two of my cases, both of them ending fatally, and the only ones so ending, death was caused by the perforation of a second ulcer. In Case II of perforated duodenal ulcer, a second perforation was found in the same viscus, while in Case III, in which the primary condition had been a perforated ulcer of the stomach, death resulted from the subsequent perforation of a duodenal ulcer. Ulcers evidently about to perforate should be treated as if they had already done so.

When we have found the seat of perforation, several methods of closure are open to us. It is my usual course to invaginate the ulcer as far as it is possible without occluding the lumen of the bowel, and then to sew all layers with a continuous catgut suture, repeated, if it is thought necessary, to strengthen it. To make the closure tight, it is then completed by a continuous Lembert suture of fine linen thread. I do not believe it is essential to cut away the edges of the ulcer. If invagination is complete, the sloughing edges will separate into the lumen of the bowel when healing takes place.

Eve[1] has lately suggested that the ulcerated area be excised by a longitudinal diamond-shaped incision, such as is used in pyloroplasty, and that the wound be then closed in the vertical direction, thus effectually avoiding narrowing the gut. In cases where such a narrowing seems especially likely, this method might be of use, but I have not as yet found it necessary.

When we have dealt with what appears to be the only perforation present we should investigate the viscus carefully to see if there is not another perforation. Gastric ulcers are multiple in about 8 per cent. of all cases; duodenal ulcers less frequently so; and perforations may also be multiple. Even when an ulcer has not yet perforated, it may be on the verge of doing so, and in that case we should deal with it exactly as if the perforation had already taken place. It must be remembered also that gastric and duodenal ulcers may exist coincidently, as in Case III, reported previously.

Adequate drainage is of the utmost importance. When the ulcers have been closed, provided that gastro-enterostomy has not been done, the peritoneal cavity may be cleaned in the immediate neighborhood of the field of operation by mild swabbing with gauze pads. I do not believe that irrigation of the whole peritoneal cavity is ever necessary or even advisable. At its best it cannot fail to disseminate infectious material, though not necessarily spreading infection. With proper drainage and modern postoperative methods, we are far safer in allowing the peritoneum to take care of itself. Irrigation may do good—it has often done harm—and the chances for the latter overbalance the possibilities of its beneficial action.

We are often best able to insert our permanent or postoperative drain before the gauze packs have been removed. Our drainage should do two things: Drain the original site of infection. This is best done by a rubber tube containing gauze, with plain gauze about, if necessary placed through, the incision itself. This may be replaced by a stab wound to one side of the incision, allowing the latter to be closed in its entirety and thus, perhaps, making the abdominal wall stronger. The choice must rest upon the judgment of the surgeon.

[1] Lancet, London, 1908, i, 1822.

Körte[1] states that he considers a drain, as a rule, unnecessary, but uses a pelvic drain where any drainage is indicated. I believe that we are usually safer in draining at the original site of infection. As the fluids of the upper abdomen always gravitate toward the pelvis, and particularly when we aid them in doing so by raising the patient in the bed, we should never force the pelvic peritoneum to deal unaided with the infectious material covering it. In all cases of severe, upper abdominal infection which might spread I employ a glass tube drain placed into the pelvis through a suprapubic stab wound, and leave it in for two or three days until all danger of general peritonitis is past.

The question of gastro-enterostomy is one of great importance and is being largely discussed by surgeons today. Deaver and others claim that the drainage thus provided, be it temporary or permanent, will permit healing of the ulcer which may exist and thus prevent the liability to secondary perforation. Mayo and Moynihan do not advocate the procedure unless the lumen of the pylorus or duodenum is seriously diminished, as they claim that in the presence of a normally patulous duodenum or pylorus the artificial gastro-enteric opening will not functionate, and thus the object sought for will not be accomplished; and, as the operation takes time and must be done on a patient who is already hard hit, it to this extent lessens the patient's chance of recovery. This problem is like so many more in surgery in that it can and should be used in certain cases and is strongly contraindicated in others, and its successful use depends on the judgment of the surgeon.

The after-treatment of perforated ulcer consists in rest for the part involved by the avoidance of food ingestion and peristalsis, and by the use of appropriate measures of defence for the peritoneum.

The patient occupies the high Fowler position so that the infectious fluid may gravitate from the absorptive diaphragmatic area to the safer pelvic zone. No fluid is given by mouth for thirty-six hours, and the patient is kept thereafter on a liquid diet and semifluid for eighteen days. The Murphy method of giving saline by enteroclysis is employed routinely; otherwise the treatment is that

[1] Loc. cit.

of any section case for a grave lesion. Vomiting, and even nausea, if at all persistent, should be treated by lavage and repeated as often as it is necessary permanently to relieve vomiting.

DISCUSSION.

Dr. John B. Roberts: I do not think this paper ought to be allowed to pass without a word being said in favor of the methods which it suggests. All surgeons should realize the importance of immediate operation and prompt drainage in cases where it is possible to give the benefit of operation to patients. I think we shall all endeavor to follow Dr. Ross' advice, if we have not already done so in our practice.

MOVING PICTURE ILLUSTRATIONS OF THE GAIT, STATION, TREMORS, AND GENERAL SYMPTOMS OF VARIOUS FORMS OF NERVOUS DISEASE.[1]

By T. H. WEISENBURG, M.D.

THE use of moving picture illustrations in medicine is of comparatively recent origin, as moving pictures were only first developed about ten years ago. Their first medical use was made by Prof. Doyen, of Paris, who illustrated a gynecological operation. These pictures were shown in most of the medical centres of Europe, but were not very good.

In this country medical moving pictures were first shown by Dr. Chase, of Boston, who exhibited his pictures in the College of Physicians in 1906 (?). His subject consisted of epileptics and cases of tic. Besides this, only one other attempt has been made by a German physician to show nervous diseases.

The present series of pictures and those that are to follow represent the first systematic attempt made to show all the different symptoms and diseases of the nervous system, as it is the purpose of the author to show everything that is possible to be shown in the realm of nervous symptomatology. The pictures shown at the present time consist of Huntingdon's chorea, generalized tic, tic of the tongue and face, astasia abasia, steppage gait, multiple neuritis, hemiplegia, multiple sclerosis, pseudomuscular dystrophy, locomotor ataxia, besides the method of taking reflexes, such as the tendon reflexes and the Babinski phenomenon.

It is hardly necessary to dilate upon the great advantage these pictures offer for teaching medical students, inasmuch as the

teacher has always at his command illustrations of certain diseases. Besides, it is psychologically interesting that the student pays more attention to what he sees when illustrated in this manner than by actually seeing the patient. Again, it is of scientific interest, inasmuch as by the photographs it is possible to detect certain phenomena which are impossible to be seen by the eye.

FATAL VASOMOTOR GANGRENE, PROBABLY DUE TO RAYNAUD'S DISEASE.[1]

By ROBERT N. WILLSON, M.D.

THERE is no pathological or clinical condition more interesting than peripheral gangrene, and in none is there more room for doubt, at times, with regard to the ultimate cause of the degenerative process. Cardiac thrombosis with embolism, the so-called thrombo-angiitis obliterans, the spontaneous gangrene of the Germans, or the series of vasomotor changes seen in Raynaud's disease—one and all of these may supply a clinical picture resembling in certain features that under discussion in the following brief report. It may well be noted that true cardiac thrombosis is a rare condition. Welch has emphasized the tendency to call postmortem thrombi by an antemortem name. To produce a true cardiac thrombus there must be present first a distinct endocardial (valvular or mural) lesion, also a retardation of the blood current, and, probably, a decided toxic increase and excess of the agglutinin constituents of the blood.

In the condition termed thrombo-angiitis obliterans there is a proliferation of the tissues of the intima which has been termed by von Winiwarter "endarteritis obliterans." In this state there are often present the symptoms of an intermittent claudication, with indefinite pains, with blanching of the skin, and with absence of pulsation in the arteries of the foot and leg, or of the hand and arm. Oftentimes, as in the spontaneous gangrene secondary to true thrombotic processes, a hemorrhagic bleb appears near the nail of the great toe, the gangrene making its start apparently from this point. Von Winiwarter ascribed these changes to the

proliferation of the intima of the vessels, resulting in their closure. Von Manteuffel concludes that this explanation is not satisfactory and proposes arteriosclerosis and a localized thrombotic process secondary to desquamation of endothelium in the popliteal artery extending directly to the periphery. Buerger differs again and claims that there is present a true thrombotic process, and not an obliterating endarteritis. He cites several cases the arteries of which seem to show the presence of a true thrombo-angiitis with organization and canalization, whereas there was nothing in these cases to indicate the correctness of the theories of von Winiwarter and von Manteuffel. Goepp[1] reports a case of this type and characterizes it as Raynaud's disease, though in the pathological report by Dr. Kelly it is distinctly stated: "The cause of this obliteration is an extensive thrombosis, apparently recent in character, and—there is in conjunction a marked periarteritis. Continuing to the very small branches there is found a marked arteriosclerosis in places, with complete occlusion and canalization." This case should be placed among those of spontaneous gangrene collected by Decker and Ellis, attributed even by von Winiwarter to thrombotic inflammation and not to Raynaud's disease. They review the literature and find 73 cases, 69 of males and 4 of female, which seem to be of this type. They report[2] a case of general arterial thrombosis in which the toes had been "black and blue" for a month, when "the pain disappeared and the toes regained their normal color. Since then he has had such attacks at intervals of about a month. The toes of the left foot have recently become black and are very painful." At autopsy the great toe and the fourth toe were gangrenous, and the other toes on the left foot were all discolored. The heart contained no thrombi. The lungs presented fresh infarctions, the spleen was full of infarcts of earlier origin and of different ages. The vessels of the kidney were thrombosed and sometimes filled by organized fibrous connective tissue. In the foot the vessels were seen through superficial section to be thrombosed, and sometimes filled by organized fibrous connective tissue; the thrombi were canalized, and in some instances had undergone hyaline degeneration. No dissection of the vessels was allowed. Dexter and Ellis claim

[1] Pennsylvania Med. Jour., April 10.   [2] Cleveland Med. Jour., April, 1910.

that their case was one of general arterial thrombosis, identical with the condition termed by the Germans spontaneous gangrene.

In certain respects the case described in this paper resembled the foregoing. In both there was a long-continued cyanosis, and a gradually developing gangrene of the extremities. In both instances the cold extremities became warm, and the natural color returned as though the causal influence had been momentarily set aside. Fortunately, in my patient the opportunity was afforded of obtaining by dissection the arteries leading into and supplying the gangrenous extremities. In no instance could either obliteration or thrombotic process be discovered. As is often the case, the anterior tibial and the posterior tibial were small, and the dorsalis pedis spread out into a fan-shaped division of tiny vessels supplying the dorsum of the foot. Nowhere was the arterial tree obstructed, however, and nowhere was there an explanation afforded for the gangrenous process other than upon the supposition that the case was one of Raynaud's disease, and unless the active cause of the gangrene was to be found in a peripheral vasomotor constriction, with consequent starvation and gangrenous degeneration of the extremities and of the tip of the nose. There was considerable antemortem doubt regarding the factor primarily and directly responsible for the extensive and rapidly oncoming gangrene. Even upon the autopsy table this doubt was not altogether dispelled. Indeed owing to the presence of thrombi (by no means certainly, though possibly antemortem) in both the right and left ventricular cavities, the arrow seemed to point toward a thrombotic etiology. Fortunately, a second autopsy was permitted before the embalming, and the opportunity was welcomed of dissecting out the right and left anterior and posterior tibials, and the dorsalis pedis, and the plantar arteries. The result of their exposure has already been described as one of entirely negative finding. Neither thrombus nor embolus nor even a high grade of sclerosis was present.

The patient, G. B., aged fifty-three years, was admitted to the wards of the Philadelphia General Hospital on March 31, 1911, in a condition almost of collapse. His face was extremely pallid and emaciated. His wife stated that he had had a cough, with night sweats, and gradual loss

of weight, extending over many years. His family history was negative. In his personal history there was neither rheumatism, typhoid, nor any serious illness. He denied venereal infection. He used alcohol and tobacco moderately. He began to feel weak and to lose weight and strength six months ago, but walked about until three weeks before admission.

The physical examination showed no abnormality referable to the osseous or muscular systems. The arteries were moderately sclerosed. The reflexes were all normal. The left lung showed considerable impairment of resonance to percussion, and many crackling rales over the upper lobe posteriorly, especially beneath the midscapula. The liver appeared hard and sclerotic, rather small than enlarged, and seemed to be completely placed below the costal margin. On April 2, 1911, a few hemorrhagic purpura appeared on the radial side of the right forearm and arm. On April 3, 1911, a small purpuric area became noticeable upon the tip of the nose. The right hand was even at this time cold and cyanotic. On April 4, 1911, both feet were also cold and blue, especially the right. On April 5, 1911, the right hand and foot became warm and nearly normal in color, resembling the left hand, which had not as yet been involved. The patient was mentally clear, but could recall no previous similar involvement of the extremities. On April 6, 1911, the patient became unconscious, the right hand and both feet showed distinct signs of gangrenous change, the nasal tip smelled distinctly fetid, the left ear margin was discolored, and Cheyne-Stokes' respiration supervened. On April 8, 1911, a small hemorrhagic bleb appeared on the left foot above the inner malleolus. On April 9, 1911, the bleb had become gangrenous, and was undergoing rapid ulcerative extension. On April 9, 1911, both feet, the right hand, and the nose were distinctly gangrenous. On April 9, 1911, the patient died, with no return to consciousness since the first onset of the Cheyne-Stokes' respiration (Fig. 1).

During the last four days of life he was incontinent of both urine and feces. The temperature was either normal or subnormal throughout the course of his sojourn in the hospital, the pulse averaged 100 to 110, and the respirations 25 (during the last few hours, 40). The urine contained throughout large quantities of albumin, and the microscope showed many granular casts of all kinds, few hyaline casts, and scattered red blood corpuscles. The sputum, which was at first profuse, contained no tubercle bacilli.

The differential leukocyte count showed slight poikilocytosis, no nucleation of red corpuscles, polymorphonuclear neutrophiles, 90.3 per cent.; large mononuclear lymphocytes, 3.7 per cent.; small lymphocytes, 3.2 per cent.; eosinophiles, 0.2 per cent., and myelocytes, 2.4 per cent.

The autopsy was performed on the day of death (April 11, 1911).

The heart was found dilated, and clots (pale, white thrombi) were present in both the right and left ventricles. Infarcts were noted in the middle lobe of the right lung and in the left kidney. The right kidney, the spleen,

and the left lung showed no signs of embolism. The left lung, however, presented old adhesions, also an area of old consolidation, partly calcified, and considerable active congestion. The aorta showed just above the

bifurcation into the iliacs a large atheromatous ulcer. The vascular system elsewhere showed little if any pathological change.

This case is instructive from more than one standpoint. Not the least interesting feature is the entire absence of necropsy findings, arterial and

venous, to bear out the suggestion of peripheral thrombo-angiitis or embolism, seemingly justified at first by both the cardiac thrombi and the infarction of the lung and kidney. Although no examination was made of the bloodvessels at the time of the main autopsy, the peripheral vessels were dissected out on the same evening, and at no point could there be found any obstruction to the lumen, either in the arms or in the legs (Fig. 2). On section the radial artery from the right arm (the right hand showing the most extensive gangrenous change) presented merely a slight proliferation of the intima and media such as would ordinarily be expected in a moderate degree of sclerosis. One of the purpuric areas was also excised from the outer surface of the thigh. On section and microscopic examination this showed a simple extravasation of blood (red corpuscles) beneath the epidermis, but no gangrenous change.

One fact immediately attracts the attention of the student of the literature of the last thirty years, namely, that there have been and are being described as instances of Raynaud's disease many cases that are actually examples of thrombo-angiitis;[1] also that there are at least occasional instances of genuine Raynaud's disease that are being attributed to embolic and thrombotic influence. It is fair to state that had this case been reported on the basis of the first incomplete autopsy, and upon its findings alone, one must have felt obliged to conclude that an embolic etiology was the one of necessity if not of choice. Yet the clinical picture, especially the complete temporary relief from arterial obstruction, also the involvement of the tip of the nose and the margin of the ear, and the absence of any marked degree of sclerosis of the vessels—these features, while not excluding, pointed most vigorously away from embolism as the likely cause of the peripheral gangrene. Even the purpuric onset does not militate against such a conclusion. Munro calls attention to a number of instances in which Raynaud's disease was ushered in by the appearance of a crop of hemorrhagic purpura. Raynaud[2] himself refers to epithelial gangrenous blisters that may break down and leave an ulcer in their place. Osler quotes a case reported by Weeks,[3] in which purpuric blotches developed before the gangrene. Many writers on the subject cite instances in which the

[1] Arteritis Obliterans, Munro, 1899, p. 134.   [2] Thesis, p. 20.
[3] Medicosurgical Bulletin, July 1, 1894

tip of the nose and the helix of the ear have become gangrenous, and have either separated in dry gangrene or required removal. Raynaud[1] himself knew of but had not seen such a case. Not invariably are these purpuric blotches true extravasations. Frequently they are accompanied by, if they do not actually consist of, a superficial gangrene of the papillary layer of the skin.

Raynaud's disease "practically never causes death," says Munro in his valuable monograph (1899, p. 109). On the basis of this assertion the case under discussion should not be included in the category of Raynaud's disease. In the absence of any other discoverable factor to explain the condition, however, we are inclined to consider the rule as not applying in this individual instance. Very many cases certainly do recover following the separation of the gangrenous parts. In some of these the general health has at no time been impaired. In others the indisposition is as persistent as it is severe and early in appearance. Presuppose, for an instant its occurrence in a patient otherwise little able to withstand a serious attack of any nature, as in nephritis (present in this case) cardiac disease, or one of the acute infections, and the fatality might follow readily enough. This patient not only gave evidence of an advanced renal degeneration, but of a more than possible tuberculosis of the left lung.

That the case represented a vasomotor neurosis of some type; that the neurosis found its causal influence in either an endogenous or exogenous toxin, acting, in the main, peripherally; and that the influence of this toxin made itself apparent in various portions of the body; these features are in line with the picture of Raynaud's disease as seen repeatedly in the experience of other reporters of cases. Adjacent portions of the body may be affected differently, as, for instance, two fingers, one of which may show the high temperature and severe cyanosis of Raynaud's asphyxia, due to overdilatation of the vessels, while the next digit presents the extreme pallor and cold of syncope. Our knowledge of the ultimate cause of the condition is scanty indeed, and sufficient only for an expression of diagnostic interest, rather than for the supplying of a means for the successful treatment of the patient.

[1] Thesis, p. 105.

Nature sometimes accomplishes that by amputating joints and minor members.

A year ago I saw a colored boy, aged nineteen years, who in two successive winters had lost portions of his fingers and toes on both feet, also the tip of his nose, and a portion of his left ear. There had been no frostbite, no pain, or any subjective discomfort, nor had there been at any time while under my observation any suggestion of diabetes or glycosuria. The extremities quietly but steadily progressed in a localized dry gangrene, which halted its own progress and left the youth maimed, to be sure, but otherwise seemingly sound. He was under observation for a number of months and during that time was free from any recurrence of the affection.

At least one cause of peripheral gangrene that can be noted in an occasional instance is a toxin introduced from without, resulting in localized vasomotor spasm fatal to the nourishment of the part. Munro cites such a case, reported by Czurda, in which "both upper arms of a child were bitten by a large spider. The arms became greatly swollen, the patient suffered severely for some weeks, and finally both hands became gangrenous and dropped off."

In a case reported very recently by Magnus,[1] the patient, a man, aged thirty-eight years, took 8 grams of male fern with castor oil for supposed tapeworm. Vomiting ensued, with violent cramps, followed by congestion of the toes and legs, and pains, and, finally, a serious paresis of one leg. He had shown for years a tendency to intermittent claudication, especially in the left leg, and in this limb occurred the most marked exaggeration of the symptoms and a very persistent paresis. The condition seemed to result directly from the action of the drug upon the vasa vasorum of the already abnormal vessels of the left leg and of the spinal cord. Musser[2] also cites an instance in a young woman in whom, following the sticking of her finger with a needle, there were violent circulatory changes in not only the injured member, but in other fingers, and later on in the feet, arms, both legs, and even the trunk. One finger and five toes have been amputated because of sloughing in gangrene. In the darkness of our present

¹ Berlin. klin. Woch., March 27, 1911.   ² Pennsylvania Med. Jour. April, 1910.

limited knowledge of the ultimate cause of the circulatory changes in the average case, and in such as that reported in this paper, especially in view of the rapidly fatal course, it may well be said that the nature of Raynaud's disease, or whatever else this patient may have suffered from, still rests in a measure of doubt. That the condition was of the order of Raynaud's disease seems very likely. That it was toxic in nature appears an equally rational conclusion. The high polymorphonuclear percentage would suggest this as beyond doubt, were there nothing else to point to its probability. There may indeed have been some degree of mural endocarditis of which the ventricular thrombi may have served as the expression; but the presence of such an infectious inflammation of the endocardium was by no means an assured fact. The crippled kidneys may also have been responsible for the retention of toxic materials manufactured in the intestinal tract or elsewhere. But the nature of the toxin, its origin, its method of onslaught, can only be surmised, and in the absence of a more detailed study of the early history of the case, extending over years instead of days previous to the terminal seizure, only generalizations and suppositions are permissible.

Even the fullest opportunity of clinical observation and laboratory investigation might have left the case in the etiological obscurity in which it now reclines.

DISCUSSION

Dr. FREDERICK P. HENRY: There is one symptom frequently present in typical cases of Raynaud's disease to which, I think, Dr. Willson has not alluded. I refer to hemoglobinuria, which was prominent in a case which I reported to the Association of American Physicians several years ago. The pathogenesis of this affection is undoubtedly obscure and possibly compound, but, in my opinion, vascular spasm is one of its principal elements. I do not think that Raynaud himself had very clear ideas upon this subject; at least, if my memory serves me, there are cases in his original monograph which, at the present day, would be excluded from the category of Raynaud's disease.

The symptom of claudicantia intermittens to which Dr. Willson alludes is more often seen in cases of arteriosclerosis of the lower extremities than in any other condition, but vasomotor spasm might, of course, be a contributing cause of it.

RADIUM.[1]

By WILLIAM S. NEWCOMET, M.D.

Radium, like the Röntgen ray, used in the treatment of disease processes in the human body requires one to be familiar with its powers and also have a consistent knowledge as to what is likely to follow each application. In this way it differs from our ordinary therapeutic agent in our medical armamentarium and therefore requires one to specialize in this direction.

Many articles have been lately written upon this subject, expressing widely different views, and at the present time it would be impossible to give an exact idea of the relative worth of this new agent. It is the purpose of this article to call attention to some points that may be of value in the relief of some distressing conditions; however, before going into detail of cases it might be to some advantage to call attention to the technique that is being used and the reasons for employing the same.

Radium is constantly giving off a series of invisible rays known as the α-, β-, and γ-rays. These rays are more or less analogous to the rays given off from an excited x-ray tube, although differing more or less widely. As for instance the γ-ray compares favorably with hard x-rays; they are not reflected or deflected by the magnet and they have great power of penetration, and although not a very active ray upon tissues they are to be desired in the treatment of deep tumors.

The β-ray is to be compared with the cathode ray of the x-ray tube, and only has a slight power of penetration; but it is a very active ray upon tissue, and like the cathode ray it is deflected by the magnet.

The α-ray has the least penetration of the three, and in the usual employment of radium need not be considered. However, when it is to be employed, the radium salt must be naked. Another method that requires considerable apparatus is where the active part of the radium salt is removed and transferred to inert substance, such as water or charcoal.

At the same time it must be remembered that in all these methods the proportion of the α-, β-, and γ-rays will differ. And this is also true of a given mass depending upon the amount of surface exposed per given weight. For instance, if the radium is in very fine powder spread over a large surface, the α-rays, not meeting with very much resistance, easily escape, and in consequence they are in larger proportion than they would be if that same mass were in a ball where the centre particles are covered and these rays are obstructed while the γ-rays still escape; thus, it is easily seen that the proportion of the different rays depend entirely upon the condition of the radium salt. There are also other variations depending upon other causes, details of which cannot be given here.

While all these facts must be taken into consideration where this agent is to be employed for its therapeutic properties, one must employ it in a manner that will meet the requirements of the many forms of cases to be treated with the greatest benefit to all; therefore, in the treatment of the cases that came under observation the radium was employed in a small capsule of aluminum, protected for the sake of cleanliness by glass covers, or where a greater effect was desired, by celluloid. Another specimen was in a glass tube. One specimen was 10 mg. of 600,000 activity, the other 1 mg. of 1,800,000 activity.

For the protection of surrounding tissues lead shields of various size and shapes were employed. And here it must not be forgotten that the radium will cause the lead to become active through secondary radiation, and these active rays in some very sensitive subjects might cause some irritation and annoyance.

When it is desired to obtain the strength of a given specimen of radium the two following methods are easy to carry out, and are not attended with the detail of those more complicated, where special training is always required.

Take two pieces of paper about one-half inch in diameter, attach each to the ends of a piece of silk thread about a foot long; this is easily done by merely cutting a small nick in the edge of each piece of paper, hang the silk thread so the two ends fall together and free from contact with any object. Take your hard rubber pen and electrically charge the pieces of paper upon the end of the thread so that they stand apart, note that they remain charged, then at a given distance hold the piece of radium to be tested and take the time required for discharge and make comparisons.

A second method is one recommended by Abbe, where a photographic plate is used and subject to a number of exposures of varying length of time and noting the deposit of silver for each unit. It gives reasonably good results, and for a working method is equal to the more accurate electroscope.

While in no manner does radium displace the x-rays in ordinary use, it will be a valuable adjunct in the treatment of cases that for some reason are not amenable to the latter form of treatment. For instance, in cases of cancer of the mouth and vagina, where it is difficult to bring the disease process directly in line with the anode of the x-ray tube, and while there have been many styles of x-ray tubes devised to insert into these cavities, none of them have been very successful. Another instance where radium seems to prove its worth is where one desires a very local application with very little exposure of the surrounding parts; and lastly, some people seem to tolerate the rays given off by radium better than those from an x-ray tube; whether this is due to some electrical discharge with the x-rays, or the fact of the greater intensity of these rays over a certain length of time, is a matter for future study.

In certain cases of carcinoma of the uterus very marked results have been observed upon the local disease, although in no manner did it seem to influence or check the metastatic processes. However, the marked change in the local condition is worth recording.

One of the most striking examples of these facts are presented in the following cases:

Mrs. M. S., aged fifty-four years. School matron by occupation. Came under observation April 28, 1908. Family history was negative. Was

the mother of four children. First was stillborn; second labor, twins; and before the last birth had one miscarriage. Menses were always profuse, but never menstruated after the last labor, which occurred when she was thirty-four years of age. With every child she suffered from an abscess of her left breast, although she could always feed her children and nourish them from· her right one. Her general health was good until about a year previous to the above date, when she began to have a discharge from the vulva, which at times contained blood; about this time she consulted her physician and operation was advised. However, for a time nothing was done, when a few months later she consulted another physician, who took her to one of our hospitals, and at this time operation was not deemed advisable on account of extensive pelvic involvement. Local treatments were then given for some months, but as conditions did not improve and the local pain became so severe, the physician advised her to try radium. Local examination at the time showed an old laceration of the perineum with a rectocele, anterior vaginal wall did not descend, uterus small and in good position, lower part fixed, with thickening toward the bladder; cervix thin, with large cup-shaped ulcer; right broad ligament was negative, while the left was much thickened, and there was a general induration of the upper vaginal walls. Bleeding was quite free after the examination, and the inguinal glands on both sides were large and tender. Histological examination made by Dr. John M. Swan of a specimen removed from the ulcerated area showed it to be an epithelioma of squamous type of cell.

Applications of radium were given three times a week, each treatment lasting for one hour.

In a few weeks there was a general improvement in all her symptoms: there was less pain, the discharge was less offensive and contained less blood; it might be stated here that the douching was continued the same as before. Local examinations were made from time to time, but very little improvement was noted, although her general health and well-being was much improved and this woman continued her work uninterruptedly, which consisted of cleaning schoolrooms.

By the end of July both general and local symptoms had improved to such an extent that the patient decided to leave the city for her vacation; she remained away about six weeks and then returned, saying that in the last few days the pain had again returned, as well as the accompanying hemorrhages. Local examination showed about the same conditions as before, except there seemed to be more encroachment upon the posterior vaginal wall. Routine treatment was again adopted, with the same general and local improvement which continued until the

following summer, when the patient decided to visit some of her friends in a neighboring city. Her vacation was, however, limited, for at the end of two weeks she again had a hemorrhage, which caused her to return home for further treatment. The following summer no vacation was taken; however, at the end of the school term she decided to give up her position, thinking if perhaps "she would take things a little easier," it might prove beneficial; at the same time she had developed a marked general cachexia; even if the local conditions had remained at least stationary, which as stated had been from time to time confirmed by several physicians.

Nothing unusual happened until early in October; the patient's stomach became rebellious and could not be controlled, the urine became choked with albumin, delirium followed, and within ten days of the woman taking to her bed, she died.

It seemed more or less remarkable, considering her arduous labors for two years· and six months from the time she was known to have an inoperable cancer of the cervix, at the same time being spared all the miseries that usually accompany this disease. The cause of death was a toxemia, the same as is observed in cases of similar disease when treated by the x-rays, where the local conditions are greatly improved, but where there is a general sapping of the system from some unknown cause.

The second case was also a neglected one—a woman who had allowed the disease to make such advances upon the uterus and surrounding parts as to render operation impossible.

Mrs. J. B., aged forty-six years, came under observation at the American Oncologic Hospital, May 29, 1909. Her general history contained nothing of interest; had seven children and two miscarriages; troubled with leucorrhea more or less her whole life; lately menses were excessive and the vaginal discharges were more offensive. Local examination showed, at that time, the vulva normal, uterus fixed, and low cervix; lacerated os admits two fingers and covered with large ulcerating nodules; fundus could not be felt, vaginal wall was indurated, but the rectum seemed to be free from disease. Some bleeding followed the examination. Treatment consisted of douchings with general tonics.

The patient's condition was so poor it was necessary to bring her into the hospital, and on November 18, 1909, it was decided to use radium for the relief of pain and its local effect upon discharges which at that time were typical of the disease. It was given for one hour daily, and continued until December 14, 1909, when the patient complained of severe pain after the treatment, and they were discontinued; during

January and February irregular treatments were given, although from March on they were given with considerable regularity, still the patient believed the radium to be the cause of her pain. However, the improvement while under treatment was so marked that it encouraged the patient to continue, and during April, May, and June the disease seemed to be more or less stationary, hemorrhage being decidedly less and the odor from the vaginal discharges could easily be controlled by douching, which before the use of the radium was impossible. During July the patient began to show a decided change for the worse, and death followed on August 2, 1910.

During the last three years there has been under observation six other cases; in all the effects of radium were about the same; that is, the local conditions remained stationary or in some improved for a time, and this gave more or less permanent relief from the severe hemorrhages and putrid vaginal discharges, in some it seemed to control the pain, and only one complained of increased pain.

Another field in which radium seems to be of value is malignant disease within the mouth. In the number of cases that have come under observation that were treated by the use of the x-rays not one of them seemed to yield the least to its effects. This fact is rather peculiar when one considers that in cases of tuberculous ulceration of the larynx the disease process usually yields easily and one sees few failures; this is also true of sarcoma. These facts lead to the trial of this new agent; and in this group of cases were included the five following: (1) A man about the middle seventies, with ulceration of the tongue and the floor of the mouth evidently started from an old leukoplakia. No result from the treatment. (2) A man, aged about seventy years; epithelioma of the epiglotis; only four treatments given. No result. (3) A man, aged about seventy years, treated for an epithelioma of the mouth for about three months; the ulceration seemed to be held in check, but then the disease seemed to advance as usual. (4) A man, aged about seventy-one years; carcinoma of the epiglottis; x-rays were first used, but had little or no effect; then radium was used, and this seemed to control the disease for about eight months. The fifth case must be given more in detail, as the result seems to be rather remarkable:

B. McC., aged fifty years, male, married, came under observation at
the American Oncologic Hospital, April 18, 1910. His general history
contained nothing of interest. About nine weeks ago he noticed a small
ulcer in the roof of his mouth. It was not painful, but it did make his
voice husky, which it had been to some extent for some time previous.
He consulted a surgeon at one of the hospitals, who tested his blood and
removed a section for examination. He advised operation, but being
informed of the gravity, he decided to consult another. The second
surgeon advised x-rays, and after a few treatments it was discontinued
and fulguration was tried; but as this was too painful he decided to change
again. About this time several of his teeth had to be removed on account
of the change in their position due to the extension of the disease. When
he came under observation there was a nodular ulceration of the soft
palate, with involvement of the left palatoglossal fold, left side of the
tongue about half its length, and the left tonsil; a few glands in the left
submaxillary region were enlarged. His general condition was good.
Radium was started as well as potassium iodide, the latter being stopped
in a few weeks, as it seemed to be of little value. The man was very
regular with his treatments, which were continued for about six months.
The ulceration healed rapidly, he gained in weight, and his general con-
dition became much better.

At the end of the time mentioned the only evidence of the disease
was a slight ulceration at the base of the tongue, and the glands in the
neck; these conditions were then corrected by operation.

DISCUSSION.

Dr. A. H. Cleveland: One of the cases to which Dr. Newcomet
referred was a patient of mine whom I saw last year about this time,
with inoperable cancer of the epiglottis, extending down the anterior
portion of the pharynx. X-ray treatment was given for, I think, three
months, with no evident improvement. The pain at that time was not
excessive, but still, sharp, lancinating pains were rather frequent. Dr.
Newcomet changed the treatment from the x-rays to the radium, and,
as he says, for eight months the improvement was marked and continuous.
The man has been absolutely without pain. The growth in the pharynx
is reduced to one-half the size, and he has lived a comparatively comfort-
able life during the last year. About four weeks ago the radium seemed
to lose its effect, and we have since stopped it. The growth is continuing,
the pain has increased markedly, and it is a question of a few weeks only,

probably, before we find the fatal result. The point that Dr. Newcomet brought out is noteworthy—that in these distinctly inoperable cases the pain is markedly lessened. In the first case, that of carcinoma of the cervix, this was a prominent feature of the treatment. The treatment in itself is absolutely without disagreeable features, and involves simply putting the tube into proximity to the affected part and holding it there for an hour at intervals. It affords great comfort to the patient, and, so far as that point is concerned, it is entirely successful.

Dr. A. B. Hirsh: I should like to hear from the writer of the paper whether he has done any work along the line of the substitutes for radium— the crude mineral, uranium, or the recently much advocated mesothorium. Mesothorium, I understand, is a by-product discovered by the Welsbach gas mantle works, in Germany, in making their mantles, and, being lower in cost, has come to be advocated as an active substitute for radium.

Dr. G. E. de Schweinitz: For the relief of pain occasioned by certain inoperable growths in and around the orbit, I have on a few occasions used radium with satisfaction, notably in one very malignant recurring carcinoma of the orbit which began in the lid and which was subjected to x-ray treatment for a long period of time without benefit. Exenteration of the orbit was performed, and for ten months the patient was entirely relieved, then recurrence took place, associated with atrocious pain, which exposure to the x-rays failed to relieve. The late Dr. Shober was called in consultation, and on three different occasions used radium, on the last of these occasions the exposure being of an hour's duration. The relief from pain was prompt and effectual, although the applications were followed by high temperature, apparently dependent upon a toxemia, so much so that the patient was desperately ill for a week or ten days. Recovery from this condition resulted, and for a long period of time the patient remained comparatively free from pain, but ultimately died of exhaustion. According to Dr. Williams, of Boston, uveal tract diseases, for example, iridocyclitis, which, as you know, are often accompanied by severe pain, are occasionally, in so far as this manifestation is concerned, relieved by radium exposure. This is mentioned as an interesting confirmation of the statement of the author of the paper that radium is at times an analgesic. Doubtless all of us are familiar with the work of Dr. Abbe, in New York, whose extensive experience in the use of radium in the treatment of epithelioma of the eyelid is well known. Certainly his published results, as well as his beautiful and artistic collection of models before and after treatment, are most remarkable. He has also used radium in the treatment of Fruehjahr's catarrh, and believes that he has secured good results.

Dr. Alfred Gordon: Radium has also been used in neurological conditions, in cases of multiple sclerosis and syringomyelia. In some peculiar way relief of symptoms is brought about. It is difficult to explain the effect in disease of the spinal cord, the relief of symptoms and arrest of atrophy, but such instances have been reported. Only a few days ago I read in foreign literature of a case in which the x-rays were used in sciatica with absolutely no result. One patient had suffered for eight months, and had had all the usual remedies and x-rays. Application of radium was made, with remarkable relief of the sciatica. It is an empirical fact, but it is so. In cases of root pain radium has given much relief. All the evidences given tonight point to the fact that pain is considerably relieved by radium. Its introduction in medical practice is very important in cases of this character.

Dr. Newcomet, closing: In reply to the question of Dr. Hirsh in regard to the use of other substances for their radio-active properties, it must be remembered that they differ widely in the character of the rays they give off, as well as the difference in quantity; therefore, some of them are very feeble, that is, from a therapeutic standpoint. For instance, one of these substances might give off a large quantity of a-rays and, not possessing the power of penetration, would not be so useful as the substance that would give off a larger proportion of β- and γ-rays. However, there is not the least doubt that some of these weaker radio-active substances, such as uranium and thorium, do possess considerable therapeutic value, and there is a need of considerable study in this direction. In most instances where radium is employed in the treatment of diseased conditions of the body it is held in some container of glass or aluminum; however, under some special conditions mica has been used; here again the low rays are to a great extent cut off, and to make it possible to obtain these rays Wickham has recommended the incorporation of the radium salt in some varnish or emulsion, thereby obtaining a large surface with little depth and very little external resistance.

The radium in our work has been confined more especially to cases where for some reason or other the x-rays seemed to have failed.

THE QUANTITATIVE ANALYSIS OF HUMAN AND OF COWS' MILK.[1]

By ARTHUR V. MEIGS, M.D., and HOWARD L. MARSH, B.S.

WE have undertaken the quantitative analysis of human milk for the purpose of proving the accuracy or inaccuracy of the analyses published by Arthur V. Meigs[2] in a paper on Milk Analysis, in 1882, and in various subsequent publications, and of cows' milk because of its great importance as a food and because it was impossible not to use it for various experiments, as it is always so easy to obtain. In the paper mentioned it was asserted "that human milk never contains more than from 0.7 to 1.5 per cent. of casein." At that time the term casein was used to designate what is now named the protein of milk. The conclusion that human milk contains only a small amount of protein, much less than had previously been supposed, was commonly accepted as a fact by physicians, and the artificial foods recommended for infants have almost all since that time been based upon the estimate that the proper amount of protein for the newborn human infant is about 1 per cent. Chemists have seemed indifferent upon the subject, and although Meigs has a number of times asked for the confirmation or refutation of the important conclusion in the twenty-nine years that have elapsed since the publication of the original paper, no one has made any investigation with a view to answering the question. Analyses have been published, and continue to be published, by chemists of repute in which the protein of human milk is estimated to be as high as 3 and even 4 per cent. It is quite unreasonable to accept as correct analyses

that rate the protein as high as 3 or 4 per cent., and at the same time to accept the conclusion of Meigs that human milk never contains more than about 1 per cent. of protein. For many years past, however, physicians have failed to perceive that the two statements are contradictory, and that if the one is correct the other is not. Most analyses have been made by determining the nitrogen by the Kjeldahl method and multiplying by a factor to ascertain the amount of protein, and the copper reduction method (Fehling's) to ascertain the amount of lactose. In many analyses direct determinations have not been made of both the protein and the lactose, but only of one of them, and the other has been estimated by difference. The reason why the determination by difference of one of the ingredients of a complex and unstable organic fluid like milk is unreliable and unscientific has been repeatedly shown by Meigs. No analysis either of human or cows' milk has heretofore been made in which the various constituents were determined gravimetrically—each one isolated from a single sample and weighed separately and the separate weights when added together shown to be equal to the weight of the original sample.

After waiting so many years, and as no one else has undertaken to solve the question at issue, we have been enabled to make an arrangement to carry out an extended study of the subject from the standpoint of pure chemistry. During the last two years we have pursued our investigations, and the junior author has devoted his entire time to the laboratory work. Dr. John Marshall, Professor of Chemistry in the University of Pennsylvania, has given us the use of his laboratory, and the work has been carried on under his supervision, and we have been guided by his advice. During the first year the work was supervised by Dr. William H. Welker, then Demonstrator of Physiological Chemistry under Prof. Marshall. While the investigation was being directed by Dr. Welker, it was carried to a point that it became evident that in human milk especially and in cows' milk to a less extent there exists a nitrogenous constituent which is not coagulable. This nitrogenous constituent does not react to any of the ordinary tests for protein.

It would have been impossible for us to have carried out the

analyses of human milk, which necessitated the use of large quantities, but for the kindness of Prof. B. C. Hirst, who placed at our disposal the facilities of the Maternity Department of the Hospital of the University of Pennsylvania. Further, we are indebted to Miss Marion E. Smith, Superintendent of the Hospital, and to her assistants who have obtained from the lying-in women as much human milk as we have required as it has been wanted.

It is important that it should be understood at the outset that in the present state of chemistry it is impossible quantitatively to analyze an organic material like milk and to obtain the accuracy of conclusion that can be had when inorganic substances are in question. It is not unreasonable to think that this will always be the case, for the component parts of milk are of composite structure instead of being simple like inorganic elements, and therefore they are liable to undergo change in the course of the manipulations of analysis. This quality makes them to a certain extent elusive. Although such accuracy as is demanded in inorganic analysis is unattainable in milk analysis, on the other hand the fat, protein, and lactose of milk are such distinctive substances that it is possible to analyze milk so accurately as to obtain results in all essential features correct.

The percentage of water was determined by the difference between the percentage of total solids and 100 parts by weight of the milk.

The total solids were determined by weighing 5 c.c. of milk in a weighed platinum dish and evaporating to dryness on a water bath. The contents of the dish were then desiccated to constant weight over sulphuric acid.

The ash was determined by slowly igniting the total solids contained in the above-mentioned weighed platinum dish. To obtain the best results the platinum dish should at no time be heated to more than a dull red glow. Sufficient heat to produce a dull red glow should be used only during the last few seconds of the ignition. A white ash was produced after about twelve hours' heating.

The determination of the fat, protein, lactose, and extractives were all made from one sample of milk. Ten c.c. of the milk

were accurately weighed into a 100 c.c. glass stoppered cylinder, and to this were added 20 c.c. of distilled water and 20 c.c. of ethyl ether, and the mixture was shaken for five minutes. Then 20 c.c. of 95 per cent. alcohol were added and this mixture was agitated for five minutes. After the cylinder had been allowed to stand a few minutes two layers separated. The upper layer consisted of an ethereal solution of all the fat, a small amount of lactose, and an infinitesimal amount of nitrogenous substance, which was soluble in alcohol, but insoluble in water and in ether alone.

The lower layer contained all of the other solid constituents of the milk.

The upper layer was removed into a weighed glass dish by means of a pipette, care being taken not to take any of the lower layer. Five c.c. of ether were added to the contents of the cylinder in such a way as to wash down the sides as well as practicable, and this was then drawn off with a pipette and discharged into the same glass dish. The washing in this manner was repeated five times to remove all the fat. The contents of the dish were then evaporated to dryness on a water bath and desiccated to constant weight over sulphuric acid. This water-free fat was treated with sufficient dry ether to dissolve it, and the solution was filtered into a small weighed beaker. After thoroughly washing the filter with dry ether the washings were added to the filtrate in the weighed beaker and the solution was evaporated and desiccated over sulphuric acid to constant weight. The residue in the beaker consisted of all the fat originally contained in the milk. The residue insoluble in ether remaining on the filter, which consisted of a very small amount of lactose (varying between 0.05 and 0.2 per cent. of the milk) and an infinitesimal amount of nitrogenous extractives, was treated with hot water, which dissolved the lactose, leaving the nitrogenous extractive on the filter. This hot water solution of lactose was added to the lower layer of milk liquid from which the protein had been removed and which contained all of the lactose except that small amount just mentioned.

The remaining portion of the contents of the cylinder, *i. e.*, the lower layer, was transferred to a 200 c.c. beaker and evaporated on a water bath to a volume of about 10 c.c.. One hundred c.c.

of 95 per cent. alcohol were then added, to bring the mixture to a content of 86 per cent. of alcohol, in order to precipitate the protein. This was allowed to stand five minutes before filtering. If allowed to stand longer than twenty minutes there is likelihood of the lactose separating by crystallization. It was then filtered through a weighed Alundum porous crucible by means of a suction pump and washed with 1 liter of boiling 86 per cent. alcohol, and subsequently with 500 c.c. of ether. As soon as the protein had been transferred to the crucible all the lumps of protein were very carefully and gently pulverized with a glass rod.

The contents of the crucible were dried at 110° C., and desiccated to constant weight over sulphuric acid. The ash content of the protein was determined by slowly igniting the contents of the crucible. The loss of weight due to the incineration represented the amount of protein.

The clear filtrate and washings from the above precipitate, to which had been added the solution in hot water of the residue derived from the ethereal solution of the fat from the original milk, was evaporated on a water bath to a small volume and transferred to a weighed platinum dish and evaporated to dryness on a water bath and desiccated to constant weight over sulphuric acid. The residue in the dish was then slowly ignited and weighed in order to determine the amount of ash. The loss in weight due to the material burned represented the amount of the lactose and extractives.

The lactose of the milk was determined by Fehling's method. The method was carried out as follows: 25 c.c. of cows' milk, or 15 c.c. in the case of human milk, or the amount of residue containing all of the lactose of the milk, together with the extractives secured from 10 c.c. of milk, were diluted to 400 c.c. in a 500 c.c. graduated flask. Fifteen c.c. of $\frac{N}{5}$ sodium hydroxide and 10 c.c. of cupric sulphate of the strength used in a Fehling's solution were added and the volume of the liquid in the flask was diluted to 500 c.c. with water.

After this mixture had been well shaken it was filtered through a dry filter into a dry flask; 100 c.c. of this solution were added to 50 c.c. of hot Fehling's solution and the mixture was boiled for six minutes. It was then quickly filtered through an Alundum

crucible and washed with about 600 c.c. of boiling water. The resulting cuprous oxide in the crucible was dissolved with nitric acid and the solution poured into the beaker which had been used in the reduction. The crucible was then thoroughly washed by passing hot water through it, and this wash water was added to the nitric acid solution which had been poured from the crucible. This nitric acid solution of the cuprous oxide was evaporated on a water bath until free from nitric acid. It was then dissolved with acetic acid and water, 8 grams of zinc acetate were added to the solution, and the liquid was transferred to a small glass-stoppered bottle; 4 grams of potassium iodide were added and the solution titrated against $\frac{N}{10}$ sodium thiosulphate with starch as an indicator.

The amount of lactose corresponding to the amount of copper found was ascertained by referring to a table given in Bulletin No. 107 (revised) of the U. S. Department of Agriculture, Bureau of Chemistry.

The amount of extractives in the milk was the difference between the lactose plus extractives and the lactose as determined by Fehling's method.

The method of Meigs for the extraction of fat from milk gave the same results as were obtained by the Soxhlet method. It has no effect upon the other constituents of the milk, and is decidedly more rapid and simpler in execution than the Soxhlet method.

The protein precipitate produced in the fat extracted milk when alcohol was added, so that the mixture contained 86 per cent. of alcohol, was all the coagulable protein of the milk. It was of high purity, as it contained only a trace of lactose and extractives. The proteins of the cows' milk and of human milk contained, respectively, 14.5043 and 13.1110 per cent. of nitrogen, corresponding to the factors 6.89 and 7.62. In calculating these nitrogen determinations the ash was in every case subtracted. The protein precipitate from cows' milk contained the larger portion of the ash of the milk, whereas the protein from human milk contained the smaller portion of the ash.

In this method of analysis we may for convenience term the fat the first fraction, the coagulable protein precipitate the second

fraction, and the remaining liquid the third fraction. This third and last fraction of the milk contained all but a very slight quantity of the lactose, a portion of the inorganic salts, and some other material of unknown composition, the presence of which chemists have recognized for many years past and have indefinitely named extractives.

Notwithstanding the use of all solvents known to us, we have failed in our attempts to quantitatively separate all of the extractives from the lactose. Our best effort succeeded in separating only about one-half of the extractives from the mixture of lactose and extractives, and this portion of extractives contained only a very slight part of the nitrogen which remained in the unextracted portion.

A part of the extractives, however, could be removed by evaporating the third fraction of the milk to a volume of approximately 1.5 c.c. and adding about 50 c.c. of methyl alcohol. At this stage difficulty was encountered in getting the solid residue derived from the 1.5 c.c. of evaporated liquid to completely dissolve in methyl alcohol. The volume to which the third fraction must be evaporated depends upon the amount of lactose present. At too great a concentration the lactose will not go into solution in methyl alcohol, and at too great a dilution the extractives will not go into solution in methyl alcohol and the lactose will not be completely precipitated when the ether is added. If unable to secure a perfect methyl alcohol solution of the lactose at the first attempt, one should concentrate and try again with different volumes.

This methyl alcohol solution was poured into 500 c.c. of dry ether contained in a glass-stoppered cylinder and violently shaken for five minutes. All the lactose and most of the nitrogen and extractives separated in large flocculi. The mixture was allowed to stand twelve hours and was then filtered through a dry filter. By evaporating the filtrate a small portion of the extractives was secured. The extractive matter thus obtained was insoluble in water but readily soluble in ethyl alcohol, chloroform, and ether. By slow evaporation from an absolute alcohol solution a very small amount of minute yellow crystals having a sharp melting point of 115° C. was obtained. The crystals when observed under the microscope had the appearance of double wedges.

By the methods described above the following results were obtained:

	Cows' milk. Per cent.		Human milk. Per cent.	
Water	88.279		87.569	
Fat	3.032		3.087	
Protein	2.942		1.481	
Lactose	4.482	} 5.085	6.574	} 7.574
Extractives	0.603		1.000	
Ash	0.733		0.252	
Total .	100.071		99.963	
Experimental error	0.071		0.037	
	100.000		100.000	

What advance can we claim to have made? Our method is an advance upon previous analyses, because after taking one sample of milk to determine the water, total solids, and ash in the usual way, we then from one other sample of the same milk take out first the fat and then the protein and weigh them, each one by itself. Afterward what remains is dried and weighed; there is, therefore, no chance for loss. This residue contains the lactose, with some salts and a material which contains nitrogen. The nitrogenous material we have been unable to isolate, and of its nature we know little except that it has solubilities similar to those of lactose. Whether it is in combination with the lactose, or if it simply remains with the lactose because its solubilities are similar, we do not know. All that it has been possible to do has been to test the residue by Fehling's method, the best now known, to ascertain the amount of lactose present, and to ascertain the amount of nitrogen by the Kjeldahl method.

The methods of analysis heretofore ordinarily used have all been more or less indirect. The determination of water, total solids, fat, and inorganic material can be said to be certainly correct except that the amount of salts is underestimated because incineration must cause some change and loss, but this is probably a small error. The lactose and protein and the material of unknown nature, whose presence is acknowledged because of the universal use of the term extractives to describe it, have all been determined indirectly. In many published analyses only the lactose or the protein has been determined, and the other one calculated by difference. The protein is generally estimated by

the Kjeldahl method for the determination of nitrogen. So far as the determination of the nitrogen is concerned it is accurate, but as there is always nitrogen present in the extractives, there is no way of finding out for certain what factor should be used to multiply the nitrogen amount in order to ascertain the quantity of protein. Fehling's test for lactose cannot be said to yield results which are certainly reliable when the solution of lactose contains other substances which might increase or diminish the copper reduction, and this is always the case in milk analysis. The truth about it, therefore, should be acknowledged that it is the best test for lactose at present known to science, but that the results obtained from its employment in any new field are to some extent uncertain. Some idea of the difficulty of dealing with lactose and of testing it may be had from the statement that we have never succeeded in obtaining a sample of absolutely nitrogen-free lactose. The best that can be purchased always contains a small amount of nitrogen, and even Merck's lactose, after having been dissolved and recrystallized five or six times, still contained a minute amount of nitrogen. By our method the fat is more easily and accurately obtained than by any other. The protein also is better separated. No reagents except volatile fluids—ether, alcohol, and water— are added to the milk, and at no time is sufficiently high temperature used to change any of the component parts. The residues are not yellow or gummy, as milk residues are so prone to become. The protein when obtained by itself is a white powder. After the fat and protein have been completely removed from a single sample of milk the remaining portion, which has been named the third fraction, contains the lactose, part of the salts, and a material or materials which for a long time have been spoken of by chemists as extractives. The problem that remains is to find some solvent or something else that will make it possible to separate in a pure state from this third fraction the lactose or the extractives. Our efforts to do this have as yet been unsuccessful, although a part of the extractives have been separated by precipitating with ether, as has been described. The precipitated portion of the extractives thus obtained contains, as has been said, a crystallizable substance whose nature we do not recognize, but whose presence in milk has been heretofore unknown. It has been

obtained only in such minute quantities that it has been impossible as yet to make any conclusive study of it.

From the point of view of the physician the results of the analysis of human milk are important in that they seem to prove the essential correctness of the conclusion reached many years ago from the analyses made by Meigs that the amount of protein in human milk is always small, only about 1 per cent., and to confirm also the conclusion that human milk does not change very greatly during the course of lactation. We have analyzed a good many samples of human milk, both samples of milk from one woman and samples of the mixed milk of a number of women, and have never found any that contained much more than 1 per cent. of protein, nor have we found any reason to think that human milk changes greatly in quantitative composition during the course of lactation. The milk of a woman whose baby is six months old does not seem to be materially different from that of a woman whose baby is one month old. In the writings upon the subject of the composition of human milk it is often assumed that the milk becomes stronger as lactation progresses. Therefore, physicians generally advise that in artificially feeding infants the food be increased in strength from week to week and from month to month. There is no good reason to think that in the lower animals the milk strengthens from month to month during lactation. The young calf probably obtains more milk as the weeks go by because the cow yields an increasing amount up to a certain point, but it does not increase in strength. If the young animal does not obtain sufficient nourishment by sucking its mother, or some other form of nourishment is desirable, it obtains this by picking up small quantities of the same foods as are eaten by its mother. A parallel to this would seem to indicate that in the artificial feeding of infants their principal food, which in civilized countries is made in imitation of human milk, should not be increased in strength from week to week and from month to month, as is commonly taught, but should be given in the same strength but in increased quantities during the first few months of life. This method has been advised by Meigs upon various occasions, and especially in an article published in 1902.[1]

[1] Analysis of Human Milk the Basis of the Artificial Feeding of Infants, TRANSACTIONS OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA, 1902, xxiv, 136.

Most of the resemblances and differences between human and cows' milk are in a general way pretty well known, but on the other hand information upon the subject has not been formulated and recorded so that it is easily accessible to physicians. It is important that everyone who is concerned in directing the artificial feeding of infants should be accurately informed in this regard. Human milk is the best food for infants, and it must therefore be imitated, and cows' milk forms the basis of almost all of the artificial foods used. The amounts of water, total solids, and fat are not very different in the two kinds of milk. The average amount of water is a little higher and the total solids a little lower in human than in cows' milk, but the difference is not great. Fat is perhaps a little higher in cows' than in human milk, but this difference also is slight. (By a curious chance the two completed analyses that we give contradict our statement in regard to the slight differences between the amounts of water, total solids, and fat generally found when human and cows' milk are compared.)

Most common cows give small percentages of fat, and there are a great many more common than there are high-grade butter cows. The amount of fat, therefore, is perhaps little if any higher in average cows' than in human milk. In artificial feeding the difference in the fat percentages, if there be any, may safely be ignored. It is in the amounts of water, total solids, and fat, therefore, that cows' and human milk resemble one another. The differences are in the percentage of ash, protein, and lactose. The percentage of ash, which is the salts, is about three times as great in cows' as in human milk. This difference is so well known that it is not necessary to dwell upon it. The differences between cows' and human milk that are of importance are those of the percentages of protein and lactose. The importance of these differences lies in the fact that they are not at the present time known by everyone to exist, and because, assuming that their existence is certain, the food value and the digestibility and possibility of assimilation of the two kinds of milk must be very different. This, if true, makes it certain that pure cows' and pure human milk cannot safely be interchangeably used as food for infants. That pure cows' milk is not a proper food for the young

human infant is now almost universally accepted by physicians in the civilized world to be a fact. The general acceptance by physicians as correct of analyses which rate the percentage of protein in human milk as high as 3 or even 4 per cent. shows that the differences of the two kinds of milk in the percentages of protein and lactose contained are not known and understood as they should be. An examination of the figures of our analyses shows at a glance the difference in the percentage of protein and lactose. In human milk the protein is much lower and the lactose much higher than in cows' milk. It is a curious fact that the sums of the amounts of protein and lactose in human and cows' milk when they are added together are nearly equal. The way in which this fact of the equality of the sums of the amounts of protein and lactose in human and cows' milk has been the cause of the failure for many years of an attainment of a general understanding of the composition of human milk was long ago pointed out by Meigs in a paper called "Proof that Human Milk Never Contains More than about One Per Cent. of Casein."[1] It was stated at the beginning of this paper that the principal reason the work was undertaken was to show the accuracy or inaccuracy of analyses of human milk that were published many years ago. It does seem to us that the evidence brought to light by two years of work at the subject comes very near to proving that those analyses are in all essential particulars so nearly correct that the generalizations drawn from them should be accepted. It is as a guide to an understanding of the best method for the artificial feeding of infants, when unfortunately they must be artificially fed, that an accurate knowledge of the relative composition of human and cows' milk has its greatest value. It is upon this knowledge alone that must be based any reasonable understanding of the subject, and without it infants can be artificially fed only as the result of experiment.

[1] TRANSACTIONS OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA, 1883–84, vi, 92; and Milk Analysis and Infant Feeding, p. 38, by Arthur V. Meigs. P. Blakiston's Son & Co., Philadelphia, 1885.

DISCUSSION.

DR. JOHN MARSHALL: The analysis of a complicated mixture of substances in solution such as milk, or the analysis of a solution of soluble substances contained in the bark of a tree, is attended with very considerable difficulty. It is what might be called proximate analysis. In ordinary chemical analysis it is the object of the chemist to convert the substance into its most insoluble form by combining it with something else, weighing the compound, and from the weight calculating the amount of the substance that must have been present in the original material. Therefore, most of the quantitative operations in chemistry are indirect, and not direct determinations. If, for example, we desire to determine the quantity of barium in a substance, the barium is converted into barium sulphate, and the weight of the latter is ascertained and from it the amount of barium that must have been present in the original substance is calculated. Dr. Meigs, however, in the quantitative analysis of the milk, thought it would be better to use a proximate method of analysis by which the proximate substances or constituents of the milk might be separated as definite entities, not by combining them with other substances and determining their quantities indirectly, but to obtain them as definite entities and weigh them. In the case of the determination of the quantity of water in milk, the matter is simple, although the residue from milk after evaporation has a tendency to absorb moisture from the atmosphere. Therefore, great care is necessary in order to keep the residue from absorbing moisture.

The question of the determination of the fat has been happily settled as far as we are concerned in the case of milk, by the method suggested by Dr. Meigs years ago, namely, the extraction of the fat directly from the milk by ether. The results of the work done by Mr. Marsh show that this method is as accurate as the Soxhlet method, which requires much longer time for its execution.

We next come to the protein constituents. What is generally known as the milk protein is a mixture of various albuminous substances, the chiefest of which is casein. There are present also lactalbumin and lactglobulin, but in slight quantity, compared with casein. This casein may be precipitated by coagulation with dilute acetic acid, but there is always the chance of the acetic acid acting upon the casein and in some measure changing it. Of this we have no knowledge. Another method is to precipitate it with a liquid that merely denatures it without changing its composition. This method was the method that was employed, namely, the addition of alcohol until the percentage of the liquid reached 86 per cent. of alcohol. With this percentage of alcohol all the protein,

casein, lactalbumin, and lactglobulin in the milk is precipitated without chemical change. Of course, the question arises as to whether casein is an individual substance or whether it is a mixture of various substances. This has never been determined; it is, therefore, simply an academic question. Certainly the caseins from various sources are different in their chemical behaviour and somewhat different in their percentage of nitrogen. Here the casein was separated as casein with lactalbumin and lactglobulin, and weighed as a mixture of the three substances. Heretofore the method employed for determining the protein milk was to make a determination of the nitrogen contained in combination in the milk. This nitrogen, of course, would be derived from the casein, lactalbumin, lactglobulin, and nitrogen contained in the extractives. The quantity of nitrogen thus found is multiplied by the so-called protein factor to convert it into terms of protein. This protein factor is not an accurate factor in the quantitative determination of proteins unless the protein is an individual chemical substance and not a mixture of two or more proteins in varying quantities. The quantity of nitrogen in proteins varies from 15 to 17 per cent. The average would be 16 per cent. The protein factor heretofore generally used was obtained by dividing the number 100 by 16 (the average percentage of nitrogen in proteins), and the quotient 6.25 obtained was the factor used in multiplying the percentage of nitrogen to convert it into terms of protein. In the older literature the protein percentages therein stated were determined by this factor. This factor is quite inaccurate because the nitrogen content of the proteins varies, and it has been found by the investigation carried on by Meigs that the protein factor for the pure protein of human milk is higher than 6.25, namely, 7.62, and for the pure proteins of cows' milk, 6.89.

In the quantitative determination of lactose numerous efforts were made, lasting over many months, to separate the lactose and to weigh it as an individual substance. Difficulties arose in that the lactose always contained more or less nitrogen, enough to say that the substance was not chemically pure. It appears impracticable to prepare lactose from milk and obtain it entirely free from nitrogen-containing bodies. A sample obtained from Merck and designated as chemically pure, still contained nitrogen, even after having been recrystallized several times. Many solvents and precipitants were employed, but without good results, so that recourse was had to the determination of the lactose by means of Fehling's solution. Here one must observe various factors in making the determination, viz., the strength of the lactose solution, the time employed in performing the determination, and the dilution. All of these factors having been taken into consideration, accurate results may be obtained by the Fehling method.

The term "extractives" is employed by chemists to designate substances

of unknown composition obtained from animal or vegetable sources. They are usually present in such minute quantity, or are of such complex nature that they have resisted the efforts of chemists to exactly determine their composition. In the extractives contained in the cow's and human milk analyzed, as described by Mr. Marsh, are included a crystalline nitrogenous substance, the identity of which could not be determined. It is present in very slight quantity, and its identification must be solved by future investigation.

DR. J. P. CROZER GRIFFITH: I have listened with a great deal of interest to the paper of Dr. Meigs' and Dr. Marsh. It shows a vast amount of painstaking work, but covers matters of a technical, chemical nature which I do not feel able to discuss. In talking of the *clinical* aspect of the subject I must go farther afield than the title of the paper indicates. There are one or two points mentioned by Dr. Meigs to which I shall refer. First of all, I approve very thoroughly of what was said about the lack of any necessity of increasing the strength of the milk mixture as the child grows older. I have long believed and taught this view. Yet the reverse is also sometimes true: That often as age increases you are forced to increase the strength of the food. That is to say, the failure of the child to gain properly in weight in spite of good digestion, and other signs of hunger should be the reason for the increase of strength of food, not merely because a certain age has been attained. Then I would express my agreement with the statement of the paper that human milk, being the best food for children, should be simulated as closely as possible by an artificial mixture. That is something which I have tried for many years to do, but I must confess that in later years I have been less certain of ability thus to imitate it. The reason for this is that in any cow's milk mixture we are giving an unnatural food, and merely because it contains the same percentages of fat, lactose, and proteid material as are found in human milk does not make the foods the same, and it does not follow that the substitute food will agree. There are distinct chemical differences, as shown in the fats, butter fat of the cow being different from that of the woman; but apart from chemical tests we know that there must be biological differences, perhaps especially in the proteid matter, which chemistry will not show. Bordet, for instance, showed that you can sensitize an animal to one sort of casein, while it would not react to that from an animal of another species. Thus, even if it were proved that the casein of cows' milk and that of human milk were alike from a chemical point of view, it would still be true that they are not so in othere respects.

The question arises as to what really are the proteids of milk. There are certainly very decided differences in the amount of non-coagulable proteid, viz., whey, proteids found in human milk and cows' milk respectively. Now it has long been the practice to give whey to infants with

delicate digestion on the ground that casein was the indigestible element
of the milk. Recently one investigator has claimed that this is not the
case, but that it is the cows' milk whey which is indigestible. Many
investigators are adopting the opinion of Finkelstein that it is not the
casein in cows' milk which disagrees, and that we do not have to be
especially careful, as we formerly were, to reduce the amount given to a
low percentage. I do not feel ready yet to go to the extent which Finkel-
stein and others do, but it certainly seems certain that we have over-
estimated the importance of casein as a cause of indigestion, and not
given sufficient thought to the indigestibility of other elements of the
food, especially the fat.

Dr. Edwin E. Graham: I want to express my appreciation of the
paper of Dr. Meigs. It certainly shows an enormous amount of continu-
ous work, and I think that in the future consideration of milk analyses,
the work of Meigs will have to be classed with that of Adriance and
Koenig and Harrington.

Pediatrists will not dispute Dr. Meigs' assertion that the proper food
for infants is human milk, but I think the great interest that this paper
will arouse will be due to whatever light it may throw upon the analysis
of human milk, and how the analysis of cows' and human milk will aid
us in the artificial feeding of children.

The whole subject of artificial feeding of children will be very much
clarified if we decide at the outset whether we are trying to feed a healthy
child with normal digestion, or a delicate child who has poor digestion
as a part of its general poor health, or a child who is sick as a result of
indigestion. It is a simple matter to modify fat, proteid, and sugar for
a healthy child. It is often a very difficult problem to feed successfully a
baby who has one of the many forms of gastro-intestinal disease. Each
child must be studied separately, and, if possible, it should be determined
in each case, which element of the food the child is unable to digest, be it
fat, proteid, or sugar, or any combination of these.

The fat in cows' and human milk is present in about the same per-
centage, but it differs in chemical composition in the two milks. The fat
in cow's milk contains a greater proportion of neutral fat and a greater
proportion of volatile fatty acids. Woman's milk contains more oleic
acid. Too much fat in an infant's diet may produce vomiting or diar-
rhea, the stools being loose and green. The large, dry stools that resemble
clay, may be caused by feeding too much fat, and it must not be forgotten
that considerable fat is found normally in the stools during infancy.
Fat indigestion is quite common in infants, and the chemist could help
the clinician if he would tell us how to modify the fat of cows' milk, as
he has long ago shown us how to modify cow proteid, but so far as I know
no chemist has ever shown us how to remove from cows' milk the ingre-

dients that are in excess in the fats, and to feed those ingredients that are normally present in the fat of woman's milk. Now that fat indigestion is being so carefully studied, perhaps it will be given more consideration.

The proteid of cows' milk is present in two and one-half times the amount as is the proteid of human milk. But if we are to believe the recent studies of the Germans, caseinogen of cows' milk rarely produces indigestion in the infant. In fact, some of the German pediatrists, Finkelstein especially, has gone so far as to suggest the feeding to infants the food that is high in proteid, moderately high in fat and very low in carbohydrates. This "Eiweiss" milk is made by removing with rennet, all the curd from one quart of milk. This curd is pressed through a fine colander and added to a pint of buttermilk and a pint of water. This gives a milk of about 3 per cent. proteid, 2.5 per cent. fat, and 1.5 per cent. sugar. This is now being used extensively, and apparently with a great deal of success. If one remembers that proteid of cows' milk and mother's milk is practically absent from the stools and is not normally present in the stools, as is the fat, it seems as if this feeding of large percentages of proteid is not so irrational as it might at first appear.

We should remember the difference in the percentage of sugar in human and cows' milk. If we add lactose to our cows' milk modification, we add it for the sake of carbohydrates, not to make the cows' milk sweeter.

DR. JOHN MARSHALL: In speaking of the difference between the casein of cows' milk and that of human milk it may be said that the cleavage products obtained by the hydrolysis of cows' and of human milk by boiling with strong hydrochloric acid are qualitatively the same. No glycocoll, however, is obtained by the hydrolysis of cows' or human casein. The quantities of these cleavage products—mono- and diamino-acids—are practically the same for both cows' and human casein, except leucin, which is contained in the casein of cows' milk to the extent of 10.5 per cent., as against 8.8 per cent. in the casein of human milk.

These mono- and diamino-acids are the so-called "building stones" that go to form the albuminous tissues of the body. By diluting cows' milk with water the protein content may be reduced to correspond with the percentage found in human milk, and thus better adapt the cows' milk for infant feeding as far as its quantity of protein is concerned, but it must be borne in mind that all of the other constituents of the cows' milk are at the same time reduced in percentage by the aqueous dilution, and these diminished quantities may require the infant to consume a larger volume of the diluted cows' milk to obtain the quantities of fat and lactose corresponding to the quantities contained in a smaller volume of human milk. And then, too, may it not be possible, in the case of cows' casein, that the larger although small quantity of leucin resulting from the

hydrolysis of the casein in the digestive processes in the body have some influence in the assimilation of this particular protein.

Dr. Meigs: There is little for me to add in conclusion, except the statement that if the methods for the artificial feeding of infants are to be advanced it must be in the direction of simplicity. The chemists and clinicians who assert that there is a known difference between the fat of the milk of the woman and that of the cow speak of a thing upon which they are not fully informed. The best artificial feeding of infants is that which most closely imitates Nature's plan—by getting the same proportions of fat, protein, lactose and water that exist in woman's milk. I am speaking of babies that are not sick, when we deal with disease it may be necessary to use a very different diet. I do wish the questions could be simplified, and I am quite certain that no chemist and no clinician can at the present time justly say and prove that the differences between the fats, caseins, and carbohydrates of human and cow's milk are known, or even that there are such differences.

THE NEW RELATIONS OF ANATOMY AND CHEMISTRY.[1]

By WILLIAM S. WADSWORTH, M.D.

A DISCUSSION of the relations of two sciences necessarily must rest on some knowledge of those sciences. Perhaps no one is fully equipped, by a complete knowledge of the whole of even one of these two sciences, to finish such a discussion. I do not happen to know anyone at present who is thoroughly qualified to speak with great assurance regarding both.

My own excuse for daring to point out certain phases of the subject rests on a rather unusual series of studies and opportunities. Since the late eighties, I have endeavored to follow Chemical Philosophy; for four years I was very actively engaged in practical clinical chemistry; and for the last twelve years I have almost constantly had cases where the action of chemicals on the human body has formed a part of the problem to be solved. On the other hand, a severe course in comparative anatomy, followed by special work in physiology, and, during the last twelve years over four thousand dissections, often associated with some of our leading chemists and anatomists.

Such a discussion as we would here undertake is, of necessity, philosophical in the broadest sense, and does not depend upon small details.

We must, by way of mental preparation for such a study, shake ourselves loose from any formulæ that may have aided text-books and teachers to impress beginners, and realize something of the breadth of the horizons of these two great sciences, and something of the subdivisions of each before we will grasp the relations that have already been established or must be formed.

Each of these great groups contains sub-groups of such impor-

tance that anyone would far outreach the limits of such a paper as this. It becomes necessary for me to sketch very briefly the results of much thought, without giving all the reasons for each statement. The result will appear rather dogmatic and perhaps not be as convincing as would a book of five hundred pages where the whole matter was expounded.

These two sciences are so different in type of content that at first thought they seem hard to compare, but the present tendencies are clearly toward a common ground. The chemist is studying the structure of matter, and the anatomist is yearning for knowledge of the substances of the structure she studies. Anatomy ranges from the gross organography, where simple observation of eye and hand give simple science, with a minimum of thought, through histology, with more elaborate interpretations, and embryology, which is mostly philosophy, to cytology, which is largely speculative.

So chemistry has its similar gradations. From simple descriptive mineralogy through the chemistry known by the average student, which consists of the reactions of inorganic substances, and where thought is of less importance than observation, to the upper realms of chemical philosophy, where the theories of atoms, ions, and ultimate units of mass and structure form the body of the science.

The postulates of this paper will be (1) that anatomy is the study of the arrangement of the chemical substances in the body; (2) that chemistry studies the anatomy of matter; (3) that anatomy will be grossly incomplete until a larger knowledge of the substances that it deals with becomes part of the science; (4) that chemistry will never fully grasp the significance of the organic compounds until it becomes familiar with the laboratories in which they are made; (5) that the leaders of thought in each science are realizing these facts; (6) that the sciences follow the leaders of thought rather than those who simply relate observations.

The expansion of these postulates will necessitate some knowledge of the history of these sciences.

There was a time when all sciences were grouped under the term "natural philosophy."

There was a time when each pre-science was a separate cult, with its devotees, and each regarded the other, if at all, with little respect, and philosophy was a *tertium quid*.

These two phases of harmony and separation are very apt to recur, and might be spoken of as the alternation of generations of philosophy.

The doctrine of evolution was an interesting example of a thought (that is, philosophy) entering into the content of science, finally gaining a foothold, and then passing on to philosophy.

In each phase it produced a complete revolution of ideas about the content of the field it had invaded.

There is no one densely ignorant enough to deny the importance of this relatively new philosophy in anatomy. Embryology has come to stay. There are, however, not a few today who do not know that chemical philosophy is rapidly becoming an integral part of anatomical philosophy. I might even suggest that the term anatomical philosophy may surprise some and be unfamiliar to many.

The older anatomists were not devoid of philosophy, but the necessity of training the eye to see, the hand to cut, and the mind to think truly, had not been made clear, and observation and thought did not always go together. The advance of the sciences have been due to increasing accuracy of thought, the improvements in technique and observation being results in most instances.

Today the anatomical sciences have become unwieldy; they have gotten too large for any single mind, and they have been subdivided until there is a great gap between the anthropometrist and the cytologist.

It is perfectly clear that the new chemistry will not directly affect, at least to any great degree, the anthropometrist, but the cytologist is daily occupied with questions that are almost as important to the organic chemist as they are to him. And the experimental morphologist, who studies the conditions of structure production, is actually more concerned with chemistry than with structures.

So also in chemistry. The industrial mining plant appears to be little affected by anatomy, but even there such problems as the

structure of the animals and plants that caused the deposits of lime, ore, coal, or clay may vastly affect the chemistry of the processes in his laboratory.

The immediately apparent relation of the chemist and the anatomist are to be found in the organic series of chemical compounds. The nature of protoplasm and its derivations and the marvellous structures, chemically, that are either made or determined by the protoplasm makes the best informed wonder whether it is ultramicroscopic anatomy or true chemistry.

No explanation of isomeric compounds on the old atomic theory can be held that does not suppose molecular structure. All graphic formulæ are but an attempt at the anatomy of the substances.

Most theories of modern chemical philosophy are along some line of structural composition. These two sciences are already overlapping widely, and yet, from the conservatism of certain old subdivisions of chemistry and anatomy, little realization is to be found of this fact, and instead of a new harmony between them, the devotees of these subdivisions are actually getting farther apart rather than coming closer together.

Time will change this and it will be to the detriment of the reputations of the overconservative ones.

The time is at hand when both anatomy and chemistry must unite to lay the foundation for a new anatomy, founded on the complete study of protoplasm.

It is not enough to say that it is a "highly complex substance," any more than it would save a medical student, at examination, to similarly describe the liver.

The anatomist and the chemist must recognize the vast importance of the conception of protoplasm, as a chemical laboratory where substances are maintained, transformed, or elaborated, and that produces structures with some of these substances, while some are simply stored or eliminated.

The "ground substance" of anatomy, of organic chemistry, and of philosophy is the knowledge of protoplasm.

Embryology and cytology have carried us to this height of knowledge, and chemistry must now cap the culmination of anatomy. Nor is this to be limited to studies of primitive proto-

plasm. It must extend to the process of differentiation of proto-
plasm and the structures and substances elaborated by it.

These elaborate structures which result are chemical sub-
stances, and their natures cannot be described if we ignore their
composition.

It may, from a hasty view, be thought that I am asking physio-
logical labors of anatomy; but embryology is generally regarded
as anatomy and that surely studies the processes of structure
formation.

In fact the true anatomist uses physiology as a handmaid,
just as much as the physiologist uses anatomy as a stepping stone,
for he must know what a structure does before he can give a repu-
table description of it.

Structure without a meaning is a discredit to the morphologist,
almost as truly as it is to the physiologist. The elaborate studies
of the arteries before the discovery of the circulation of the blood
are very instructive. The names that have been tacked to some
parts and organs are fortunately not translated, or we might
be oftener impressed by their folly. The names of certain parts,
whose functions were understood, show that the use of the organ
or part, is not unsuitable knowledge for an anatomist.

Anatomy must always remain a biological science, and must
retain and maintain its proper relation with the biological sciences
for its own sake as much as for theirs.

I yield to no one in the matter of science for science's sake,
but I know, as some do not appear to know, that the pedantry
which tends to isolate any subdivision from its great group is
not thinking right and is not working in the right way to make
that branch a success.

Everyone who follows modern medicine is impressed with the
increasing importance of chemistry. In place of drugs we are
giving chemical substances; instead of gastric juice we speak of
pepsin and hydrochloric acid; we speak of urea, indican, and the
various salts rather than of the urine.

We even study the chemical composition of the blood, where
we once only watched its clotting or counted the cells. We are
beginning to take up the composition of the granules of those cells.

But we have not demanded the formal union of anatomy and

chemistry, possibly because we are dominated by the ideas regarding these sciences that were taught us in school. Surely there was good psychology in the saying, "Bring up a child in the way it should go, and when he is old he will not depart therefrom."

That injunction was not written in the interest of modern science, however.

Our medical chemistry did not prepare us for an understanding of biochemistry, and our anatomy was driven into our unwilling minds with little regard to our taking part in the thinking of modern science.

Shall these things go on in the face of knowledge and wisdom? Is all the new thought regarding the destruction of poisons in the system—toxins, antitoxins, and antibodies—to go to waste in our midst, or must we graft on our old anatomy something of modern thought?

Far better would it be if the anatomy would grow as it did under the impulse of histology and embryology, and demand of its votaries a grasp of the chemistry of the substances that are the basis of structure.

In olden times some organs were regarded as curiosities, and some were too insignificant to be mentioned, but we may rest assured that the ductless glands will receive very respectful attention of the future anatomists, and the reason is very simple, because we have learned that they are the seat of certain vastly important chemical activities.

Studies of the power of certain vital products to precipitate other vital products have aroused us to a realization that chemical ignorance is inexcusable.

The whole range of storage of presubstances that have but to issue through the mystic portals of the cell and work magic far beyond the dreams of the alchemists—for they have but to touch a substance and that substance is transformed—this whole range of preformed chemical substances is to become part of the content of anatomy.

The lesson from the almost infinite potential of the parathyroids is very different from the teachings of anthropometry.

This live little member is going to force some of our conservative

friends to take up the study of chemical philosophy, and then the marvellous vistas will open up of knowledge of systems of ions, atoms, and ultimate units that will make the solar system appear a poor, simple thing by comparison. The marvels of crystallography will be lost in the wonders of the colloids.

Medical men will be ushered into the mysteries of the chemical philosophy as a child is born into the world, and they will have to find themselves and adjust themselves to that new world, and the sooner the better.

And has poor, old, conservative anatomy got to leave its delectable corpses and rattle its old bones and get into this brain staggering complexity of form, force, unit, and increment? Perhaps not, but there will come a new, young anatomy that will have gotten in touch with chemistry from the very outset, while its mind was open and its vision clear, and chemistry will not be a thing far distant and very difficult. It will form a very great part of the substances of this new young anatomy.

Full well do I know that I will be regarded by some as visionary; but remembering what was said about the doctrine of evolution; how the cell doctrine was treated in this very town, within the memory of those still living, and how long it took to introduce chemical methods into surgery, I shall not worry over it. We have but to think of a mechanic or an architect, giving out a description of anything, from a watch to a cathedral, with no regard to the substances or materials. Then we see how very close to absurdity stands our isolated, unchemicalized anatomy.

Our city has returned to its rightful place as the centre of anatomy in the continent, and with the recent increase in the teaching of the new chemistry, I judged it a proper time to bring to the attention of the college a matter of such fundamental import.

DISCUSSION.

Dr. H. H. Donaldson, of the Wistar Institute: In the paper just presented, Dr. Wadsworth directs attention to a less usual way of contemplating the structure of the animal body. It must, of course, be looked

upon in every possible way, that is self-evident. Equally self-evident is
it that the older anatomy, so far as it is related to medicine, was in the
service of surgery, and we now desire also an anatomy in the service of
physiology.

Dr. Wadsworth has pointed out the need for a better appreciation of
this point of view, and of greater precision in our analysis of the facts.

Broadly speaking, it is common knowledge that the chemistry of the
human body differs according to *race* (skin pigments or body smells),
sex (incidence of disease and secondary sex functions), as well as *age*
(percentage of water in the entire body or varying resistance to drugs).
Moreover, it varies according to *season*, to *climate*, to *diet*, to the *daily
rhythm* of rest and activity, and to the degree of fatigue, and all of these
modifying factors are one thing in conditions of health and another in
the course of disease. A number of these factors have not yet been shown
to be of great significance, but that probably means that we have not
yet looked deeply enough into the matter.

Frogs in the spring react very differently from frogs in the autumn.
Abel has shown that the effect of acid fuchsin upon a fatigued frog is
distinctly different from that on a frog at rest, and the variations in the
action of drugs under different conditions are only too familiar.

For advancement it is desirable, therefore, to bring together these
several classes of facts and recognize the body as composed of structures
which are in a continual course of change, so far as their chemical com-
position is concerned. The adoption of this point of view is then the first
idea on which the speaker has laid emphasis.

While it is comparatively easy to admit that all this is very true, we
are often compelled to state merely that the chemical conditions of the
body have altered, without being precise as to the localities or organs
in which the alteration has occurred.

The second point is, therefore, precision in analysis. Those who have
the anatomical habit of mind can dissect the body with the eye and
visualize more or less isolated, for example, the alimentary tract, the vas-
cular system, the skeleton, or the nervous system, as the case may be,
with all the other confusing structures for the moment removed. It is
proposed to carry this one step farther—to form the habit of visualizing
the body in other terms, say the terms of iron, or water, or salts, or any
constituent which may be chosen, because by using this method we are
perforce compelled to determine where the chemical substances in which
we are interested are most abundant, and what changes they may
undergo. This I venture to call anatomy in the service of physiology.
It supplements the present situation merely by the fact of introducing
the anatomical element where the physiological one has heretofore pre-
dominated.

Let me give two instances of the application of these ideas. My colleague, Dr. Edward Meigs, finds it all important to determine the chemical composition of striped as contrasted with smooth muscle, in order to have a basis for selecting between the various explanations of their physiological peculiarities.

At this time Dr. Koch, also a colleague, is determining the make-up of the brain at different ages in the terms of its chief chemical constituents, in order to find an explanation for the growth changes which occur in it.

The description of the body in chemical terms will be an achievement of the same order as that of the older descriptions in physical terms, both useful, medically speaking, in so far as they help in some other way. The older anatomy has proved fundamental to surgery; the newer is destined to occupy much the same position toward physiology.

It seems to me, therefore, not a question of desirability in accepting such a point of view, because in essence it is already accepted, but rather a question of emphasizing and giving a value to views which are already widely held and also a question of haste in order to obtain as soon as possible the advantages of this newer knowledge.

DR. JOHN MARSHALL: I admit the desirability of understanding the composition of the substance spoken of as protoplasm, but I doubt very much whether we shall be able to obtain any considerable knowledge of the ultimate composition or structure of that substance from the anatomists who may have knowledge of the chemical composition of the soft and hard tissues of the animal body. It is also desirable that we should know how to transmute the baser metals into the more valuable ones, but the subject of the understanding of the composition of protoplasm as well as the transmutation of metals has occupied the minds of chemists for years and no answer has come to the questions. I agree with what Professor Donaldson has said with respect to the chemical part of anatomy belonging practically to physiology and being covered by physiology. It is very desirable that the anatomists should know the composition of the solid and fluid tissues of the body. It is quite likely that most anatomists have knowledge of the gross chemical composition of these structures. It is, however, a question in my mind whether the anatomist is prepared to acquire a deep knowledge of chemistry in addition to his deep knowledge of anatomy to enable him to speak with authority on the subject of the chemistry of the structures of the body.

DR. WADSWORTH: I find the usual difficulty in condensing a large subject into a short paper and yet making myself so clear that there will be no misunderstanding regarding detail. The subject is well worth the attention of a body of practical physicians because it is fundamental for the work of all physicians, no matter what the special branch in which

they are active. It is necessary for them to know the material with which they are to work. They must have such knowledge in order that their art shall be raised above the crudest empiricism.

I am but asking for reasonable beginnings along lines already established and for the introduction of methods and facts already attained.

We could not be so absurd as to ask for a finished knowledge of protoplasm at this time, but we should not be satisfied with the present status of the writing and teaching for medical students and practitioners where little more is said than that protoplasm contains O, H, C, and N in proportions that vary within certain limits.

Every day we insist on knowing more of the nature of the things we study. It is not enough to know that blood cells are granular, or that they stain with some specially prescribed fluid. We want to know whether they are acidophile, neutrophile, or basophile granules, and we will gladly accept larger knowledge as to their composition. So must we know the nature of the granules that give rise to the enzymes and other active principles associated with bodily ailments. To be very pointed, we ask for the introduction of modern methods into conservative branches that have fallen slightly behind their proper place.

The plant morphologists have long located the substances found in plants and used a well-developed microchemistry in so doing.

When I was a student of biology, I had to be able to recognize the substances in the structure of plants, and when I conducted a clinical laboratory I used some of the same reagents with most satisfactory results.

You can all see what I mean by referring to the works on materia medica, at least in part. It may be hard to have to follow the plant morphologist, but it is inexcusable to refuse to follow when the way has been opened up.

Look through your works on anatomy and you will be impressed with the lack of information to be found on the substances of and in the structures.

THE THERAPEUTIC APPLICATION OF P-HYDROXY-PHENYLETHYLAMINE (TYRAMINE).[1]

By DANIEL M. HOYT, M.D.,

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ABELOUS,[2] in 1906, noted that a rise of blood pressure was produced from the intravenous injection of the extracts of putrid meat. In 1909 Barger and Walpole[3] showed that this rise of pressure was at least in part due to certain amine substances, of which p-hydroxyphenylethylamine (tyramine) was the most active. A little later, Barger and Dale[4] announced that the powerful pressor substance contained in the watery extract of ergot was mainly p-hydroxyphenylethylamine.

There is further considerable evidence to show that this amine is formed in the human intestine from tyrosin. It was found by Langestein[5] after prolonged peptic digestion of egg albumin. Barger and Walpole[6] took two specimens of broth which were infected with a culture from human feces. To one tyrosin was added; the other was used as a control. Extracts from each were tested physiologically, and it was shown that the extract from the specimen which had contained the tyrosin produced a very marked rise of pressure, while the control produced a slight but distinct fall. Bain,[7] though the evidence presented is far from complete, has added another interesting phase to this subject by showing that in cases of high blood pressure these pressor

[1] Read December 6, 1911. [2] Soc. de Biol., May 30, 1906, i, 463.
[3] Jour. Physiol., March 22, 1909, xxxviii, No. 4.
[4] Ibid., vol. xxxviii; Proc. Physiol. Soc., May 15, 1909.
[5] Beit. Chem. Physiol. u. Path., 1902, i. 507.
[6] Jour. of Physiol., March 22, 1909, vol. xxxviii, No. 4.
[7] Lancet, 1910, clxxviii, 1190.

substances are absent from the urine, while in normal individuals they appear constantly in adult life, thus making the inference that the retention of these amines in the body is in part at least the cause of the high blood pressure. He attempted further to influence the excretion of these substances by giving the subjects medicinal doses of so-called intestinal antiseptics, and in some instances lactic acid-forming bacteria.

These procedures, however, he states have no effect upon the excretion of the pressor substances in the urine. It is to be noted that there is a distinct, though not very close, chemical relationship between these amines and adrenalin. Further, they are a constituent of two common therapeutic agents, namely, the older cod-liver oil and, as has been intimated, the watery extracts of ergot. Gautier[1] isolated the base from the mother liquors obtained from the putrefaction of cod livers. The older and darker oil, therefore, contained these, because the oil used to be extracted by a process involving putrefaction. The present product does not contain them, as it is produced by a steam process and the cod livers are not allowed to putrefy. It is still insisted by many clinicians of wide experience that the older cod-liver oil possessed a more powerful stimulating action than the present purer product, and it is noteworthy that the tendency to look upon this substance as simply a fat food rather than as a medicine has gone hand in hand with the improvements in the methods of extraction. It is, however, with the amine as obtained from ergot that this paper has particularly to deal. Dale and Dixon[2] have outlined the physiological action of this substance experimentally. Briefly, they have found that intravenous injection causes a marked, abrupt rise in blood pressure, resembling very closely that of adrenalin, save that the latent period is greater and the rise of blood pressure more prolonged, and that it is active when administered hypodermically, and by the gastro-intestinal tract. Experiments upon the isolated mammalian heart indicate that this rise of pressure is partly due to cardiac stimulation, while if

[1] Bull. Soc. Chim., 1906, iii, 35, 1195.
[2] Jour. of Physiol., July 23, 1909, vol. xxxix, No. 1.

Ringer's fluid be perfused through the isolated lung the rate of flow is not affected, indicating that there is no constriction of the pulmonary vessels. On the other hand, perfusion through a portion of the intestinal circulation, and plethysmographic experiments on the ear volume indicate that there is marked constriction peripherally of those arterioles having a vasomotor nerve supply. Upon the uterus its influence is almost identical with that of adrenalin, producing in the cat a decrease in the muscular contraction of the virgin organ and marked increase in the contraction in pregnancy. It produces dilatation of the pupil, retraction of the nictitating membrane, widening of the palpebral fissure, protrusion of the eyeball, and secretion of tears. All these effects upon the eye can be produced after the removal of the superior cervical ganglion, indicating their peripheral origin. We have then a substance that, like adrenalin, stimulates peripherally all those structures which have a sympathetic nerve supply, but is unlike it in that tyramine is more prolonged in its action, has less local effect, is less toxic, and is active when given by the mouth or hypodermically. With this summary of its physiological action, it is reasonable to suppose that here we ought to have a substance that possesses the same therapeutic value as adrenalin, with the added advantages of continuous action and lessened local effect to interfere with systemic action, and a substance which is active when administered by mouth. Of its excretion Ewins and Laidlaw[1] have shown that 25 per cent. of it may be found in the urine as parahydroxyphenylacetic acid, and that the heart muscle entirely destroys the substance.

In the paper by Dale and Dixon, already referred to, the first observation upon human blood pressure with this substance is recorded. One of the writers took 10 mg. by mouth. His pressure before taking the drug varied between 110 and 115 mm. The pressure after taking the drug was recorded every five minutes, as follows: 124, 136, 149, 148, 135, 136, 134, 134, 122 (thirty minutes' interval for a meal), 130 mm. It will be seen that a rise

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[1] Jour. Physiol., London, 1910–11, xli, 78 to 87.

is recorded five minutes after the taking of the drug, that fifteen
minutes after the pressure has risen 34 mm., and that eighty-five
minutes after there was an elevation of 15 mm. The writer
repeated the above upon himself, the blood pressure being taken
by Dr. Lucius Tuttle, of the Physiological Department of Jeffer-
son Medical School. Any psychical effect was here ruled out by
so administering the drug that neither he nor the writer knew
when the 10 mg. was taken. This was accomplished by using
two glasses containing the same amount of water, into one of
which the drug was placed. The contents of the glasses were taken
a half hour apart, and as the substance has practically no taste
in this dosage, the writer had no way of knowing when he took
the drug and when the water. The result is recorded in detail
at the end of this paper (No. 1). During the entire hour there
was at no time any rise of blood pressure, but rather a distinct
fall. The pressure at 7.45 P.M., before either dose was taken,
was 138 mm.; the pulse, 90. At 8.35 the pressure was 118;
the pulse, 88. This was eighteen minutes after the tyramine
was administered. Twenty-nine minutes after the pressure was
120; the rate, 82. The fall of pressure was probably due to the
fact that we were working in a small office and we had several
lights burning, so that the temperature of the room was constantly
growing warmer during the experiment.

In a case of chronic myocarditis 10 mg. of tyramine by the
mouth, as will be seen by referring to No. 2, was followed in
sixteen minutes by a rise of 5 mm.; twenty-nine minutes after
the pressure had risen 7 mm. Such a slight rise, however, can
hardly be looked upon as due to the drug; for a difference of
10 mm. is certainly in the range of accidental variation. One
hour and thirty-five minutes later the pressure had dropped
25 mm. This was after ingestion of a large quantity of hot soup.
In other words, in these two observations there is no evidence
that the drug taken by the mouth in 10 mg. doses has any definite
effect upon the circulation. This is not in accord with the experi-
ment of Dale and Dixon, it is probable, therefore, that this rise
of pressure was due to psychical influence, as Dr. Dale himself
thinks, and has said in a communication to the writer to that

effect. Alfred Clark,[1] working at the suggestion of Dr. Dixon, found that the administration of tyramine by the mouth to healthy individuals produced the following results:

BLOOD PRESSURE AT TWENTY-MINUTE INTERVALS AFTER ADMINISTRATION OF DRUG.

Experiment.	Subject.	Dose.	0	20	40	60	80	100	120	140	160	180
I	A. J. C.	15 mg.	105	105	100	103	103					
II	A. J. C.	30 mg.	102	105	107	107	113	112	...	117	117	110
III	H. D.	30 mg.	110	118	116	116						
IV	H. D.	50 mg.	110	118	120	118	...	120	120	...	...	112

Clark also made an observation in which he gave 100 mg. by the mouth. At 10.30 A.M. the patient's blood pressure was 105; on the previous day, 103. At 11.05, 100 mg. of tyramine was administered. At 11.40 the blood pressure was still 105. At 11.45, 100 mg. more was administered. At 12 M. the blood pressure was 103. At 12.30, after dinner, still 103; 12.40, 105; 1.40, 109; 2.20, 107; 2.30, 109; 3.30, 118; 6.30, 113. The previous day, at 6.30, the patient's blood pressure was 107.

It is evident from this study with two doses of 100 mg., given at forty-minute intervals, that not until three hours and forty-five minutes after the last dose was the blood pressure distinctly raised, it being 118 mm., while on the previous day at the same time it was 105, 13 mm. higher. If the rise was due to the drug it came on very late, and was not marked.

As to the effect upon the blood pressure of repeated doses by the mouth, the writer has not yet observed a sufficient number of cases to do more than suggest the effect. He took three cases of moderately advanced tuberculosis; one received 5 mg. three times a day, the other two 10 mg., each three times a day. The blood pressure records were made morning, noon, and night, taken at times by the writer, at times by Dr. Alexander, a resident physician at the Philadelphia Hospital, and by the head nurse. In two of these cases there was no evidence of any effect (No. 3 and No. 5). In one case there was recorded a rise of pressure of 20 mm., and the day after the drug was stopped the pressure

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[1] Biochemical Journal, vol. v, No. 5.

slowly fell. This one case is, as has already been said, only
suggestive.

The effect of hypodermic injections of small doses up to 20 mg.
is very slight (No. 19). Clark in his paper calls attention to the fact
that he found the most favorable site for systemic effect to be the
loose tissue beneath the clavicle. In one case (No. 11), where 10 mg.
were administered, there was some evidence of action, the pressure
rose 12 mm., and the strength of the heart sounds was markedly
increased; the case was one of mitral insufficiency with dilatation.
Only about half the systoles could be made out at the wrist.
After the giving of the drug there was a distinct improvement
in the character of the heart sound, particularly as to regularity
and uniformity. This effect, however, was but transitory.
These findings are in the main consistent with Clark's results;
save as already noted, he seemed to get better effect when the
drug was given in the subclavicular fossa. He also obtained a
greater local effect than the writer noticed. He speaks of pallor
and goose-flesh at once seen around the site of the injection,
followed by hyperemia; 15 mg. were followed by a rise of 6 mm.
in five minutes; 20 mg., 16 mm. When, however, you reach a
dose of 30 mg., the effect becomes very marked, but at the same
time extremely fugacious (No. 20). The plotted curve on page
271 represents the result of injecting 40 mg. subcutaneously
below the clavicle in a case of chronic myocarditis with pulmonary
tuberculosis, the patient being profoundly toxic (No. 17 a).

The diagram distinctly illustrates several important things in
regard to the action of this substance. It will be noted that four
minutes after the injection the blood pressure had risen from
85 to 130, a jump of 45 mm. This patient being toxic, it is prob-
able that the cause of the low blood pressure was in part at least
vasomotor; but so sudden was the rise of blood pressure that for
the time being it caused a distinct slowing of the heart, and
although the drug is a decided stimulant to that organ, yet the
rise of pressure was associated with a very transitory irregularity.
The next most striking thing is its marked transitory action.
From a study of the experimental curves in the lower animals,
one would expect a much more prolonged effect. In this instance

nineteen minutes after the drug was given the blood pressure had again reached the normal and the cardiac rate was practically the same. In fact, the picture is strikingly like that of the intravenous injection of adrenalin. Clark's[1] results for the larger doses again correspond closely with the writer's. An injection of 40 mg. produces a rise of blood pressure of 30 mm. in ten minutes, associated with an increase of pulse rate; an injection of 50 mg., a rise of 50 mm., accompanied by a fall in the pulse rate; an injection of 60 mg., a rise of 60 mm., again with a fall of pulse rate. These were cases with practically normal blood pressure. In three cases of shock the injection of 20, 50, and 70 mm. produced approximately the same effect as in the normal cases, save that the reaction was distinctly less marked, and in no case was there any evidence of continuousness of action.

It is well understood that the above studies are far too few to draw any definite conclusion. It is to be noted, however, that the writer has selected cases in which the blood pressure was likely to remain constant, and has avoided acute shock with its natural tendency to recovery, and that, therefore, the distinct changes which follow the administration of drug were probably due to it. Further, it will be seen that Clark and the writer, working absolutely independently, have reached practically the same conclusion as to the value of this substance as a circulatory stimulant. The drug is freely soluble in water, produces apparently no gastrointestinal irritation, and when given by the mouth is very uncertain and slow in its effect. When administered in doses from 20 to 40 mg. it produces a marked and abrupt rise of pressure, which is very fugacious and is sometimes associated with slowing of the pulse rate and irregular heart action. The substance should be of value in the treatment of conditions in which there was marked vasomotor depression, but it apparently cannot be depended upon for any prolonged action.

I wish to express my thanks to Prof. W. E. Dixon and Dr. H. H. Dale for their assistance. Also to Dr. T. Mellor Tyson, Dr. William E. Hughes, Dr. L. N. Boston, and Dr. Ward Brinton for the privilege of selecting cases from their wards.

[1] Biochemical Journal, vol. v, No. 5.

No. 1.—D. M. H.   October 19, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
7.45	138	90	Had been smoking fifteen minutes before.
7.47	. . .	. .	Took water.
7.52	138		
8.00	130	86	
8.08	120	86	
8.16	124	84	
8.17	. . .	. .	10 mg. tyramine by mouth in water.
8.22	120	84	
8.29	120	80	
8.35	118	88	
8.46	120	82	

Blood pressure taken by Dr. Lucius Tuttle.

No. 2.—W. N.   Diagnosis: Chronic myocarditis.   Men's medical, Philadelphia Hospital.   July 3, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
3.10	105	54	
3.12	105	50	
3.14	105	56	
3.19	105	54	10 mg. tyramine by mouth.
3.35	110	48	Sweating increased.
3.48	112	54	Sweating increased.
4.02	110	54	
4.04	. . .	. .	Taking supper.
4.44	80	54	
4.48	90	. .	Very free sweating.
5.30	80	62	

No. 3.—C. R.   Diagnosis: Fibroid tuberculosis with asthmatic symptoms.   Women's tuberculosis, Philadelphia Hospital.   October 4, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
3.14	120	96	
6.00 P.M.	118	92	
October 5.			
8.45 A.M.	116	94	Tyramine 0.005 gram by mouth at 8 A.M., 12 M., and 4 P.M.
3.18 P.M.	120	88	
6.00	120	88	

Time.	Blood pressure.	Pulse.	Remarks.
October 6.			
9.30 A.M.	110	140	
6.20 P.M.	122	102	
October 7.			
9.20 A.M.	114	108	
2.47 P.M.	120	110	Just came up stairs.
7.00	120	100	
October 8.			
9.40 A.M.	100	114	Just came up stairs.
3.25 P.M.	120	94	
6.30	122	96	Drug stopped.
October 9.			
9.00 A.M.	110	108	
2.25 P.M.	112	100	
6.40	120	112	
October 10.			
10.30 A.M.	108	104	
3.35 P.M.	110	130	Just been walking very fast.

No. 4. — S. G.   Diagnosis: Moderately advanced tuberculosis. Women's tuberculosis, Philadelphia Hospital.   October 4, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
October 4.			
3.50	102	80	
October 5.			
9.10 A.M.	96	88	10 mg. tyramine by mouth, 8 A.M., 12 M., and 4 P.M.
1.30 P.M.	96	90	
3.22	96	90	
3.25	92	90	
6.00	100	98	
October 6.			
9.30 A.M.	98	100	
11.15	104	94	
?	110	100	Coughing.
6.15 P.M.	112	102	
October 7.			
9.30 A.M.	108	92	
2.38 P.M.	105	90	
7.00	108	96	

Time.	Blood pressure.	Pulse.	Remarks.
October 8.			
9.50 A.M.	122	122	Drug stopped.
3.36 P.M.	120	102	
6.30	118	90	
October 9.			
9.04 A.M.	98	96	
2.30 P.M.	96	96	
6.35	116	100	
October 10.			
10.40 A.M.	98	104	
3.36 P.M.	110	110	

Was getting essence pepsin, $\frac{1}{2}$ dr.; tinct. digitalis, 10 mm.; tinct. nux vomica, 10 mm., but stopped during experiment.

No. 5. — J. S. Diagnosis: Moderately advanced tuberculosis. Women's tuberculosis, Philadelphia Hospital. October 4, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
October 4.			
3.35	120	70	
October 5.			
8.00	. . .	. . .	10 mg. tyramine, 8 A.M., 12 M., and 4 P.M.
8.30	114	82	
2.00 P.M.	98	78	
3.10	100	80	
3.15	105	76	
6.00	110	72	
October 6.			
9.30 A.M.	102	72	
11.00	120	80	
6.25 P.M.	122	72	
October 7.			
9.25 A.M.	118	76	
2.38 P.M.	120	74	
7.55	120	86	
October 8.			
9.45 A.M.	120	76	
3.26 P.M.	118	76	Drug stopped, 12 M.
6.30 P.M.	120	62	
October 9.			
9.08 A.M.	120	70	
2.28 P.M.	110	84	
6.45	110	82	

Time.	Blood pressure.	Pulse.	Remarks.
October 10.			
10.35 A.M.	112	88	
3.27 P.M.	112	84	

Has been getting nux vomica, 7 min.; soda bicarb. 7 gr.; tinct. gentian, q. s. ad 1 fluidram. Was stopped during experiment.

No. 6.—F. D.   Tuberculous pneumonia; practically moribund; died that night.   April 14. 1911.

Time.	Blood pressure.	Pulse.	Remarks.
3.27	70	124	
3.33.5	. . .	. . .	5 mg. tyramine hypodermically.
3.35	80	124	
3.40	72	128	
3.45	80	128	
3.48	80	130	
3.53	82	136	
3.57	80	140	
4.00	85	126	
4.03	. . .	130	
4.05	73	140	
	78	110	Head lifted.
	. . .	130	
4.15	80	70	Sat up suddenly.

No. 7.—C. H.   Diagnosis: Advanced tuberculosis, left-sided effusion. April 18, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
3.05 P.M.	110	124	Nervous.
3.09	110	122	
3.10	108	124	
3.13	102	124	
3.14	102	122	Talking.
3.21	112	126	
3.38	112	122	
3.40	112	118	
3.43	114	124	Nervous.
3.44	110		
3.48	. .	. . .	5 mg. tyramine hypodermically in leg, deep.

Time.	Blood pressure.	Pulse.	Remarks.
3.50.5	110	124	
3.55	110	118	
4.03	100	118	
4.04	110		
4.05	103	120	
4.08	108	112	
4.46	90	112	Had supper.
4.48	90	118	
4.50	98	120	

No. 8.—A. M. Diagnosis: Pulmonary tuberculosis; ascites; dilated heart. Men's medical, Philadelphia Hospital.

Time.	Blood pressure.	Pulse.	Remarks.
2.05 P.M.	108	110	Nervous.
2.15	120	. . .	Heart sounds 128 to 130.
2.19	. . .	. . .	0.005 gram tyramine hypodermic-ally.
2.21	119	120	
2.25	. . .	115	
2.26	. . .	122	
2.29	114	120	
2.37	108	110	
2.38	116	112	

Has been getting caffeine citrate, 5 grains; nux vomica, 5 minims, three times a day. States that the night following the injection the sleeping and breathing improved.

No. 9.—M. G. Diagnosis: Bronchopneumonia. Men's medical, Philadelphia Hospital. July 1, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
2.02.5 P.M.	100	76	
2.08	102	80	
2.15	95–100	78	
2.16	. . .	. . .	0.005 gm. tyramine hypodermic-ally.
2.19	90	78	
2.28	80	74	
2.40	90	74	Nervous. Free sweating.
2.50	90	68	
2.58	95	68	
3.04	88	74	

No. 10.—S. H. Diagnosis: Gastritis; exhaustion. Men's medical, Philadelphia Hospital.

Time.	Blood pressure.	Pulse.	Remarks.
2.28 P.M.	100	96	Repeated observations.
2.35	. . .	. . .	10 mg. tyramine intermuscularly.
2.36	. . .	90	
2.39	100	94	
2.42	100	96	
2.48	100	92	
2.50	100	92	
2.53	98	96	
2.58	98	92	
3.06	103	96	
3.54	95	88	Free sweating.

No. 11.—James McF. Diagnosis: Myocarditis; mitral regurgitation. Philadelphia Hospital. July 3, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
4.17 P.M.	120	70	Heart very irregular; about one-half of the systoles reach wrist.
4.30	120	70	Heart very irregular; about one-half of the systoles reach wrist.
4.32	. . .	. . .	10 mg. tyramine hypodermically; deep.
4.37	120	60	Heart irregular.
4.52	132	76	Heart more regular and larger percentage of beats felt at wrist. Heart sound apparently stronger, pulse improved.
4.59	130	78	
5.02	132	78	
5.15	112	72	
5.21.5	120	70	Been getting strychnine sulph., $\frac{1}{30}$ gr. t. i. d.
July 15.		.	
1.13 P.M.	118	90	Pulse very irregular.
11.30	. . .	. . .	10 mg. tyramine three times a day for three doses.
July 16.			
2.15 P.M.	115	88	Very irregular.

No. 12.—G. W. H.—Diagnosis: Cirrhosis of liver; pleural effusion.
Men's medical, Presbyterian Hospital.   July 13, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
1.35 P.M.	135	88	
1.44	140	80	Nervous.
1.46	140	90	
2.03	. . .	. . .	10 mg. tyramine hypodermically.
2.06	138	90	
2.12	140	96	
2.17	138	88	Skin more moist.
2.20	142	84	
2.23	135	88	
2.29	140	86	Complains of heat.
2.33	140	88	Complains of heat, sweating freely.
2.40	140	88	
2.46	130	84	Face flushed.
2.53	130	86	
?	140	92	

No. 13.—J. B.   Weight, 103.   Diagnosis: Hodgkin's disease.   Presbyterian Hospital.

Time.	Blood pressure.	Pulse.	Remarks.
3.25	108	68	
3.28	105	64	
3.30	105	64	
3.40	. . .	. . .	Tyramine subcutaneously, 10 mg.
3.45	105	60	Drinks glass of milk; sits up to do it.
3.47	. . .	. . .	Lies down.
3.49	108	64	Skin very moist.
3.53	102	. . .	Nervous and worried about domestic affairs. Talking about same.
3.54	108	64	
3.57	108	64	Slight irregularity.
4.01.5	102	72	Complains of heat.
4.32	110	66	Talking with minister.
4.38	108	66	Service going on in ward.
4.42	110	64	
4.45	108	64	

No. 14. —John S. Diagnosis: Fibroid heart, acute gastro-enteritis.
Presbyterian Hospital. July 19, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
2.10	110	80	
2.14	110	76	Taking glass of albumin water.
2.16	110	80	
2.53	. . .	. . .	15 mg. tyramine deep under skin below angle of scapula; cuff taken off and put back.
2.55	102	70	
3.00	102	72	
3.05	100	80	
3.10	105	82	
3.15	110	76	
3.20	110	80	
3.25	110	82	
3.30	110	76	

No. 15.—H. K. Diagnosis: Hysteria. July 18, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
12.10	130	66	
12.12	120	72	.
12.15	118	66	
12.18	112	68	
12.27	120	66	
12.35	. . .	. . .	20 mg. tyramine in leg hypodermically.
12.40	115	74	Nervous.
12.45	125	74	Talking.
12.50	123	76	Skin moist.
12.55	125	88	
1.00 P.M.	120	78	
1.05	115	72	
1.10	120	76	
1.15	110	72	
1.18	122	72	

No. 16.—W. G. Diagnosis: Acute alcoholism. Men's medical,
Philadelphia Hospital. July 17, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
2.30	123	88	Low muttering delirium.
2.34	123	96	Coughing.

Time.	Blood pressure.	Pulse.	Remarks.
2.35	123	90	Coughing.
2.37	123	100	Coughing.
2.38	123	96	
3.08	. . .	. . .	20 mg. tyramine hypodermically; leg.
3.12	130	90	
3.15	130	90	
3.20	132	94	Coughing.
3.25	120	96	
3.30	128	88	Coughing.
3.38	123	96	
3.40	130	100	
3.49	120	100	

Has been making efforts to get out of bed. Been getting sodii brom., gr. xxx; chloral. hyd., gr. v; inf. digitalis, ½ fluidounce; strych. sulph., gr. 140 t. i. d.

No. 17.— M. O.   Diagnosis: Advanced tuberculosis; great circulatory weakness.   Women's tuberculosis, Philadelphia Hospital.   September 25, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
11.37	85	88	Pain over heart.
11.38	85		
11.40	90	90	After coughing.
11.53	85	84	After coughing.
11.56	. . .	. . .	40 mg. tyramine, subclavicular fossa.
11.58	112	86	
12.00	130	80	Heart irregular, local puckering pallor.
12.02	135	86	Heart irregular, complains of pain over heart.
12.06	130	96	Heart more regular.
12.07.5	118	104	After coughing.
12.10	98	98	
12.12	92	92	
12.15	85	94	Coughing.
12.18	88	92	
12.21	85	94	
12.23	85	88	Heart regular.

No. 17a.—M. Q.   Diagnosis: Advanced tuberculosis; marked circulatory weakness.   Women's tuberculosis, Philadelphia Hospital.
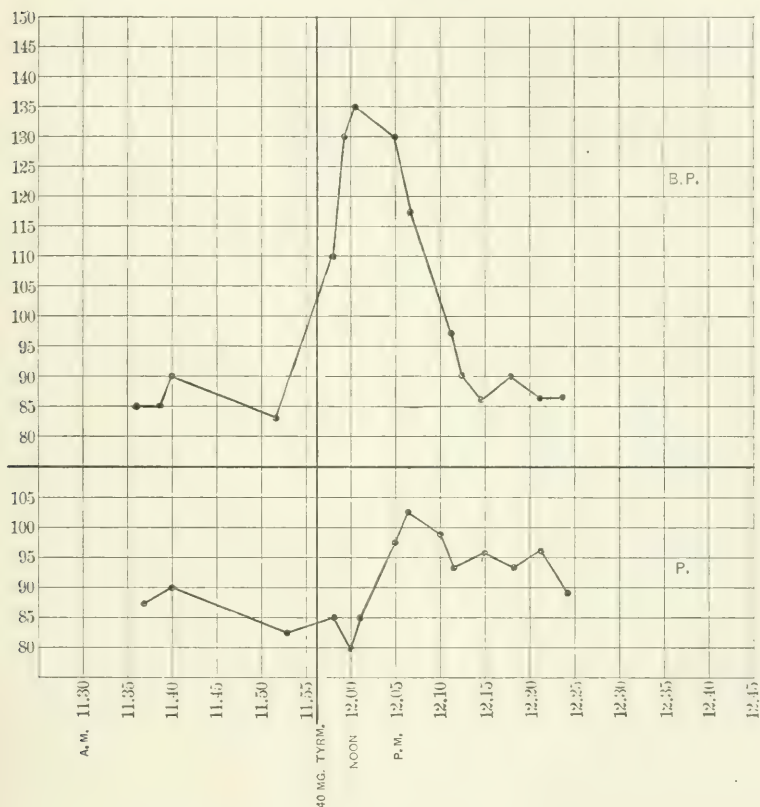
No. 18. —T. K.   Diagnosis: Advanced tuberculosis; failing circulation. May 17, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
5.49	75	128	
5.52	75	128	Tyramine 1.5 mg. intravenously.
6.03	70	126	
6.06	70	132	
6.09	75	128	Coughing.
6.12	70	128	
6.14	75	128	Coughing; dyspnea.

Time.	Blood pressure.	Pulse.	Remarks.
6.25	. . .	140	
6.27	80	138	
6.29	80	132	Dyspnea.
6.31	80	130	
	. . .	112	
6.35	70	134	Died May 21, 1911.

No. 19.—T. Men's tuberculosis. November 29, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
11.56 A.M.	114	100	
11.58	112	108	
11.59	112	104	
12.02 P.M.	114	88	
12.03	. . .	. . .	20 mg. tyramine, subclavian fossa, subcutaneously.
12.05	112	108	
12.06	124	104	
12.07	122	108	
12.08	122	108	
12.10	116	108	

No. 20.—Men's tuberculosis, Philadelphia Hospital. November 29, 1911.

Time.	Blood pressure.	Pulse.	Remarks.
11.05 A.M.	120	88	
11.07	122	100	
11.11	120	102	
11.14	. . .	. . .	30 mg. tyramine, subclavian fossa, subcutaneously.
11.17	130	92	
11.20	150	88	
11.21	150	96	
11.23	145	90	
11.25	140	88	
11.27	128	92	
11.29	130	92	
11.32	118	96	
11.35	120	94	
11.38	. . .	96	

DISCUSSION.

Dr. JOSEPH SAILER: The paper of Dr. Hoyt has touched upon some subjects which are rather difficult of solution at the present day. In the first place it arouses our interest in the mechanism of prolonged deviations from the normal blood pressure. I do not think that at the present time we have any satisfactory explanation as to why in certain cases the blood pressure is persistently and abnormally high. I think it has been shown by Fraenkel, Miller, and others that in chronic interstitial nephritis with high blood pressure an excess of adrenalin has not been found. On the other hand, we would not expect high blood pressure, as in exophthalmic goitre, if this or similar substances are present.

It is possible also that there are developed substances in the body as the result of pathological processes which may be supplied to the circulation and continuously serve to increase the blood pressure. At the present time there is a very unsatisfactory condition of therapeutics in reference to high blood pressure, and to low pressure as well. As Dr. Hoyt has shown, the substance that he has studied is inefficient. It may be of value in acute states, but in chronic states, it is as futile as any of the other remedies.

Dr. HOYT, closing: I have nothing to add except to state that the reason for selecting cases of this type, that is, cases in which there was some circulatory weakness of a chronic nature, was that I could thus determine how long the substance really acted. Ergot has been recommended in the treatment of circulatory failure by many clinicians. Tyramine represents the active principle of ergot which is soluble in water, ergotoxine being the other important active substance. Its physiological effect resembles tyramine.

THE EHRLICH REMEDY IN THE TREATMENT OF SYPHILIS.[1]

By JUDSON DALAND, M.D.,

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SALVARSAN is not only an important but a permanent addition to our means of combating syphilis. In certain cases it produces results most brilliant and not otherwise attainable. This drug, though at first administered solely intramuscularly, is now given almost always intravenously.

The ordinary intravenous dose for an adult is 0.5 gram; for an adolescent, 0.3 to 0.4 gram, and for the newborn infant, 0.01 gram. In general paresis, cerebral syphilis, and tabes dorsalis it is wiser to employ at first but 0.4 gram. Later this dose may be increased to 0.5 gram. In advanced diseases of the nervous and cardiovascular systems, salvarsan is contraindicated. Nevertheless, in a few cases brilliant results have been secured by injecting 0.2 gram in sterile oil suspension into each gluteal muscle. I have administered as much as 0.5 or 0.6 gram intravenously to children seven or eight years of age, suffering from congenital syphilis, without toxicity and with therapeutic benefit. Intramuscularly, I have given 0.9 gram to a case of paresis without toxicity and unfortunately without benefit. Almost all competent observers agree with Professor Ehrlich that salvarsan acts best when administered intravenously. The following method for the intravenous injection of salvarsan has proved satisfactory.

The 0.5 or 0.6 gram of salvarsan contained in the glass tube is placed in a sterile 25 c.c. graduate, to which are added 19 c.c. of hot *sterile* normal salt solution, and shaken vigorously until complete solution is secured. Under sterile conditions add,

drop by drop, shaking vigorously each time, a 20 per cent. solution of sodium hydroxide until the base has been entirely precipitated; and this procedure continued until the precipitate is redissolved, care being taken that no *excess* of sodium hydroxide is added. The solution should be alkaline, transparent, and pale sherry in color. It should be strained through gauze, added to 130 c.c. of sterile normal salt solution at a temperature of 110° F. and placed in a water bath so as to maintain this temperature. A modification of Weintraud's apparatus, made by George P. Pilling & Son, of Philadelphia, is sterilized, and 40 c.c. of hot normal salt solution introduced into the glass reservoir and allowed to fill and warm the rubber tube, all air being expelled by allowing this solution to flow from the needle until but 10 c.c. remain in the reservoir. After the vein has been overdistended by a tourniquet, the needle is introduced in the direction of the blood current, the tourniquet immediately removed, and the 10 c.c. of normal salt solution remaining in the reservoir is allowed to flow. If the solution flows freely and no swelling appears in the neighborhood of the vein, it demonstrates that the needle is within the vein. If the solution does not flow, or flows slowly, or there is slight swelling, it is evident that the needle is not within the vein, and necessitates exposure of the vein by dissection.

If the needle has been properly introduced, the arsenobenzol solution is then poured into the reservoir and allowed to flow into the vein at a rate not exceeding 20 c.c. per sixty seconds. The rate of flow is regulated by raising or lowering the glass reservoir. Whenever possible a large vein should be selected so that the arsenobenzol solution will be diluted by a large quantity of flowing blood, thereby preventing the local effect of the drug upon the vein, *i. e.*, acute phlebitis and thrombosis.

When the vein is deeply situated or invisible, or if the needle cannot be successfully introduced into the vein through the skin, the vein should be exposed by dissection; and a curved needle is safer and more convenient. The needle should be carefully held in its original position during the injection so as

to avoid displacement or injury to the vein. The vein, which is frequently quite movable, should be held securely in place by the lateral pressure of the index finger and thumb; and the patient should remain absolutely motionless, as even a slight movement of *any* part of the body may dislodge the needle from the lumen of the vein. When the solution of salvarsan has almost disappeared from the reservoir, the rubber tube should be compressed and 20 c.c. of hot normal salt solution introduced into the reservoir and allowed to flow slowly through the tube, needle, and vein, following the arsenobenzol solution, until but 10 c.c. remain. If the cubic contents of the rubber tube is 10 c.c., the additional 10 c.c. will wash all the salvarsan from the needle and vein, thus preventing local injury, as this solution is an intense chemical irritant. The needle is then withdrawn, pressure applied, and adhesive plaster is the only dressing necessary.

As 0.6 gram of salvarsan is dissolved in 150 c.c. of hot distilled normal salt solution, each 25 c.c. is the equivalent of 0.1 gram of the drug, so that any dose less than the maximum may be easily calculated.

Complete sterility is absolutely necessary, and the intravenous injection is best given in a hospital with the aid of two assistants and a nurse. All apparatus and solutions should be sterilized immediately before the operation, and this is especially true of the physiological salt solution.

As a rule, the patient experiences no unpleasant sensations during the injection; but occasionally there is suffusion of the eyes and face, cardiac palpitation or irregularity, vertigo or nausea. The occurrence of any of these symptoms is an indication that the injection should be suspended. When the injection has been completed, the patient should remain recumbent, make no muscular effort, and remain under a physician's observation for at least half an hour. In a few cases, soon after the injection, one or more of the following symptoms may occur: headache, nausea, vomiting, muscular or intestinal cramps, or diarrhea. The temperature occasionally rises to 100° or 102° F., with or without chills. Professor Ehrlich believes that most of

these symptoms will be obviated if the normal salt solution is sterilized immediately before the operation; but my experience is opposed to this view.

The after-management of patients who have received salvarsan intravenously varies. All should remain in bed the first twenty-four hours. In syphilis of the nervous or cardiovascular system or viscera, the patient should, in addition, remain in his room in bed or in a chair the second twenty-four hours. The third day he may move quietly about the hospital and afterward return home, and do no important mental or physical work for four days. These directions, so far as the second and third days are concerned, are of less importance and may be omitted in ordinary, uncomplicated cases of primary or secondary syphilis.

The advantages of the intravenous over all other methods of administering the Ehrlich remedy are, that the full dose of the drug circulates in the blood at one time, and thereby exerts its maximum spirillicide action, with, as a rule, no discomfort to the patient. The dangers from the intravenous injection of the Ehrlich remedy are: (1) Emboli from air or blood clot; (2) syncope; (3) convulsions or collapse, especially in paresis and luetic cardiovascular disease.

The amount and rate of absorption of the drug is always uncertain when administered intramuscularly, and severe pain often occurs followed by more or less infiltration, which is often exceedingly painful, and occasionally terminates in a sterile abscess from necrosis of the muscle. In marked chlorosis, anemia, or malnutrition these painful infiltrations may remain several weeks.

In disease of the nervous or cardiovascular system, where doubt exists as to the extent of the disease, or the wisdom of using salvarsan, and in asthenia and emaciation, the intramuscular injection is to be preferred. The dose and method of making the alkaline solution for the intramuscular method is the same as that used in the intravenous method, excepting that the total volume is but 20 c.c., one-half being injected into the right, and the other half into the left gluteal muscle, which muscles are the best for the purpose. The drug may be made into a neutral

emulsion by the so-called Wechselman method; or it may be suspended in paraffin or sterile olive oil; or made into an alkaline solution, which is more rapidly and surely absorbed and may be preferred, despite the fact that it causes more pain. In patients who are weak, or where caution is necessary, the drug may be administered as a sterile oil emulsion, prepared as follows:

Place the salvarsan in a sterile agate or glass mortar and add thereto, slowly, drop by drop, 8 or 9 c.c. of a recently sterilized olive oil, which should be continuously and thoroughly rubbed into the powder by means of a pestle, so that ultimately an emulsion, cream-like in appearance, is secured. This emulsion is drawn into a sterile syringe, the skin over the site of the puncture sterilized, and the needle introduced into the centre of the contracted gluteal muscle. As soon as the injection is completed the muscle should be relaxed and gentle massage applied and adhesive plaster placed over the puncture. Should pain or swelling occur, hot normal salt fomentations or hot magnesium sulphate may be applied, or, if necessary, morphine hypodermically.

In most cases the drug is erroneously introduced into the fat over the gluteal muscle in the neighborhood of the sciatic notch, thus interferring with absorption, causing unnecessary pain and infiltration, and not infrequently inflammation of the sciatic nerve from the local chemical irritant action of the remedy.

Professor Ehrlich's hope, based upon animal experimentation, that salvarsan would sterilize a syphilitic by one dose, is no longer entertained, although therapie sterilisans magna is possible in certain cases of primary syphilis. In most cases, however, the dose should be repeated in one week; and in tertiary, para- and congenital syphilis, additional doses are usually necessary. In primary syphilis the Spirochetæ pallida disappear from the chancre within twenty-four hours, as is true in animals in which a similar process has been induced experimentally. If the Wassermann reaction remains persistently negative for a period of two or more years, the patient may be viewed as being free from disease; if, however, the Wassermann reaction becomes strongly

positive, an injection should be given at once, and repeated until the serodiagnostic test becomes negative.

Naturally, the most favorable cases for treatment are the recent fresh infections; and as soon as the spirochete or the Wassermann reaction demonstrates the existence of a chancre, it should be excised if possible, with the idea of removing surgically as much of the infected material as possible, so that the remedy may address itself to the parasites existing in the lymphatics, blood, and other parts of the body. After the administration of salvarsan, usually within twenty-four hours no spirochetes are discoverable; and in forty-eight hours the chancre usually presents the appearance of a clean, punched-out ulcer, which rapidly heals.

In the ordinary forms of secondary syphilis two injections should be given at an interval of seven days; and four weeks later, if the Wassermann reaction is positive, a third injection, the endeavor being to secure a persistently negative serum reaction to syphilis.

Tertiary and congenital syphilis, as well as syphilis of the nervous system, may require several injections; and the patient should simultaneously receive the benefit of mercury and the iodides.

The contraindications to the use of the Ehrlich remedy are as follows: Advanced syphilitic myocarditis; advanced syphilitic disease of the aorta or coronary arteries, or aneurysm; syphilitic aortic insufficiency; hemiplegia from ruptured syphilitic artery; advanced general paresis; advanced disseminated sclerosis; advanced tabes dorsalis; extreme debility or emaciation.

A number of deaths have followed the administration of the Ehrlich remedy and the reports of the autopsies are most instructive. Some were moribund when injected; one overworked physically the day after the injection and died a cardiovascular death. Most of the deaths, however, were due to advanced syphilis of the bloodvessels, more especially the aorta, with aortic insufficiency and syphilitic myocarditis. In about one-half of these cases these pathological conditions were not recognized during life. It is, therefore, evident that in all cases of long-standing syphilis a complete physical and general exami-

nation is necessary. One death occurred in a case of terminal diabetes mellitus, although benefit may be expected in early cases, syphilitic in origin.

A complication following the administration of salvarsan, which had aroused much discussion, is the occurrence of lesions of the optic, auditory, and other cranial and peripheral nerves. At present the preponderance of testimony is in favor of the supposition that these cases are examples of syphilitic relapses and are not due to arsenobenzol. Relatively, these cases are few in number; but absolutely, they have been recently more frequently observed than in the past.

The nerve most commonly affected is the auditory, and next in frequency is the optic. The ophthalmoscopic appearances in general conform more closely to the picture of syphilis rather than arsenic. In the present imperfect state of our knowledge it is impossible to formulate a definite, positive opinion; but I incline personally to the belief that although most of these cases of cranial nerve involvement are syphilitic relapses, a small percentage are in some way induced by salvarsan. Some observers believe that salvarsan induces a predisposition to these complications. Prior to the administration of salvarsan certain of these nerves may be slightly syphilitic, but not sufficiently to cause signs or symptoms, and, when the drug is injected, may produce a transitory hyperemia and swelling, precisely as is observed in old, dry inactive tertiary lesions of the skin. In view of the occasional involvement, more especially of the auditory and optic nerves, I believe that each case of advanced syphilis should be examined as to the integrity of these nerves before using the Ehrlich remedy. A complete physical and general examination, a urinalysis and a blood pressure observation should be made before injecting salvarsan. In hypertension or plethora a preliminary venesection is desirable. In cardiac weakness all physical and mental strain should be avoided, and the volume of the diluted arsenobenzol reduced to a minimum.

The indications for the use of the Ehrlich remedy are: (1) Cases refractory to mercury; (2) cases but partially improved by mercury; (3) cases showing an idiosyncrasy to mercury,

whereby therapeutic inefficient doses produce mercurialism; (4) infective lesions occurring in prostitutes, or the ignorant and careless; prompt treatment usually renders such patients non-infective within twenty-four hours; (5) the results in primary syphilis have been satisfactory, the local lesion usually healing promptly, as a rule, much more rapidly than from the use of mercury. In one case but a single injection was necessary. In secondary syphilis similarly good results were frequently obtained, mucous patches usually quickly disappearing; likewise ulcerations of the mouth, tongue, and throat. The extreme pain and salivation accompanying these ulcerations disappeared in less than twenty-four hours.

The most brilliant results were obtained in certain cases of tertiary syphilis, as, for example, a gumma of the arm, which had resisted treatment for several months, in a few days showed healthy granulations and was soon healed. In a case of ulcerations of the face and neck, which had resisted mercury for nearly two years, in twenty-four hours showed marked hyperemia and swelling, healthy granulations soon appeared, so that healing was accomplished in a few weeks. A case of osteomyelitis of the tibia, which had received temporary relief by two surgical operations, relapsed, despite the continued use of mercury, and for nearly a year suffered continuously from severe, almost unbearable pains, preventing sleep, which pains entirely disappeared in fourteen hours after the injection of 0.6 gram of salvarsan intravenously, and a similar quantity intramuscularly. When the last report was received, four months later, the pain had not returned. A similar result was observed in an old woman suffering from syphilitic caries of the cranium.

A brilliant result was observed in the case of a male, aged fifty years, almost moribund, profoundly emaciated, and adynamic, with extreme thickening of the peripheral arteries and a thick psoriaform mass upon the right tibia. Under the influence of 0.4 gram of sterile oil emulsion of salvarsan introduced into the gluteal muscles, he rapidly gained in strength and color, and in a few days the psoriaform mass became detached, leaving a healthy skin beneath; and in the course of a month a gain

of 22 pounds in weight was secured. The results in several cases of general paresis have been, on the whole, unsatisfactory. Dr. Francis X. Dercum has observed one case of early paresis favorably influenced by salvarsan, and Dr. Isaac Leopold has made a similar observation.

The lancinating pains of tabes dorsalis are usually aggravated after the administration of salvarsan for from twenty-four to forty-eight hours, and then marked improvement or cessation of the pains usually occurs. Although in many cases of locomotor ataxia, no especial benefit, apart from the cessation of pains or disappearance of crises, could be demonstrated in the comparatively short time that they were under observation, it is encouraging to note that in one case, which was under observation thirteen months, while under the influence of salvarsan given intravenously, a W.$+++$ was replaced by a W.$-$, which endured for almost four months, and was replaced by a W.$++$, and after the last injection a negative phase was again secured. The behavior of the serum reaction for syphilis in this case, in my judgment, is evidence that the etiological factors, *i. e.*, the Spirochæte pallida and its toxins, have been controlled and the disease brought to a standstill. Symptomatically, there has been a disappearance of pains, improvement in general health and marked diminution of ataxia. The following symptoms remained unchanged: (1) Unequal pupils; (2) loss of knee-jerk; (3) loss of sexual power.

Dr. Francis X. Dercum has had similar results in a case under observation for a similar period of time, with the exception that his patient showed an extraordinary gain in muscular coördination.

It is impossible at present to formulate definitely the exact value of salvarsan in tabes dorsalis; but the remedy should be advised in cases showing a strongly positive Wassermann reaction, with the object of bringing the syphilitic process to a standstill by causing the destruction of the Spirochæte pallida and securing a negative serodiagnostic test for syphilis. If an incurable and progressive disease, such as locomotor ataxia, can be arrested, no more should be expected, as the nerve structures destroyed cannot be replaced.

Despite the fact that salvarsan is contraindicated in advanced paresis, advanced locomotor ataxia, and syphilitic endarteritis, I have experimentally employed salvarsan in these cases and have observed no ill effect; but, on the contrary, in a few instances, have observed excellent results.   If hypertension exists it should be reduced, especially in cardiovascular disease, and the quantity of the solution should be as small as possible, and introduced very slowly.

The results observed in congenital syphilitic choroiditis have, on the whole, been only partially satisfactory.

It is acknowledged that the only method by which syphilis can be diagnosticated, in the absence of signs or symptoms, is by the Wassermann reaction; and it is my belief that the presence of a positive serum reaction, in a case of syphilis where all symptoms and signs have disappeared, is evidence that there still exist Spirocheta pallida in numbers sufficient to make the antibodies that give a positive serum reaction, and, therefore, these patients are liable to relapses, or to the development later of serious diseases, such as paresis, tabes, aortic diseases, aneurysm, degeneration of the myocardium.

Experience has shown that it is sometimes difficult to maintain continuously a negative Wassermann reaction.   Ordinarily a negative serum reaction is secured, but in one, two, or four months is replaced by a positive reaction if the disease is well advanced, the patient showing no signs or symptoms of syphilis and apparently in good health.   Usually, such cases should have received a second intravenous injection within one week, and later a third or fourth.   Naturally, many of these patients disappear and desire no further advice; but in the present state of our knowledge it is urgently necessary that advanced syphilis should be treated vigorously not only with salvarsan, but also with mercury and the iodides, with the object of attacking the disease simultaneously from all sides, thereby securing the prompt disappearance of lesions and a permanent negative Wassermann reaction.   Hitherto, in order to study the effect of salvarsan, all cases of syphilis have been treated by the Ehrlich remedy alone.

THE THERAPEUTIC RESULTS FROM THE USE OF DIOXYDIAMIDOARSENOBENZOL IN TWENTY-ONE CASES OF SYPHILIS.[1]

By JAY FRANK SCHAMBERG, M.D.,

AND

NATE GINSBURG, M.D.

(With quantitative determinations of arsenic in the urine of two of the cases by Leon A. Ryan, M.D., of the University of Pennsylvania.)

THE genius of Ehrlich and the technical skill of his able assistants, Hata and Bertheim, have brought into existence a scientific synthetic drug for the treatment of syphilis which continues to hold the attention of the medical profession. Although 20,000 persons have now been treated with the Ehrlich preparation, and although an already voluminous literature on the subject has accumulated, a much longer probational period will be necessary before we shall have acquired knowledge sufficient to pronounce a definite and complete verdict on the value of this remedy. Improvements in technique are being published from time to time, and the most recent pronouncement is, like the railroad time-table, "subject to change." Nevertheless, much has been learned—sufficient to convince the most skeptical that an epochal advance in the therapeutics of syphilis, and, indeed, in therapeutics generally, has been made.

Ehrlich has, with the magic wand of the master alchemist, transformed a highly poisonous inorganic substance into an organic substance relatively non-toxic for the human economy, but

[1] Read January 4, 1911.

lethal for the spiral germs of syphilis. Ehrlich says that the combination of the arsenic with the benzol radical lessens the toxicity of the drug, and increases the spirillocidal activity. The introduction of the halogen group (iodine for example) in the arsenophenol, increases the spirillocide effect, but decreases the trypanosomicide influence to almost zero.

TOXICITY. Wechselmann in his treatment of 1400 cases states that he did not witness a single case of arsenic poisoning, and claims that no such accident has yet taken place. In autopsies that have been made upon patients treated by this method and dying from some other cause, there has been no evidence published of the poisonous effects of arsenic upon the tissues. This is all the more remarkable in view of the fact that arsenobenzol contains 34 per cent. of arsenic, and is given in doses varying between 5 and 15 grains.

It must not be concluded, however, from these statements that arsenobenzol is a perfectly harmless compound; it is quite possible that we may yet learn of serious complications following its use in persons highly susceptible to the drug, and in others in whom the technique has been somewhat faulty.

ELIMINATION. Arsenic is rapidly eliminated in the urine and a little more slowly in the feces. The results are somewhat discrepant as to the duration of the elimination, but in a general way it may be stated that in persons with sound kidneys nearly all of the arsenic is eliminated in from twelve to fourteen days. The elimination is more rapid in cases in which the intravenous injections have been given. With the subcutaneous and intramuscular injections some residue of the arsenic will be found at the site of the injection for a considerable period of time. There is seen here an analogy with the injection of insoluble preparations of mercury.

METHOD OF ADMINISTRATION. While there is at the present time no complete unanimity of sentiment as to the best method of administration, there is a preponderant opinion that the drug given by the intravenous route has the most prompt influence upon the existing lesions, and makes the most profound influence

upon the disease itself. Inasmuch, however, as elimination takes place very rapidly by this method, many European observers are counselling the intravenous injections, to be followed after some days either by a second intravenous injection or by a subcutaneous injection. Ehrlich, himself, believes that the intravenous injections are the most effective. Wechselmann, on the other hand, states, after using this method in 100 cases, that he is not convinced that its effects are superior to the subcutaneous administration which he has employed over 1500 times.

In using the *intravenous injections*, a weak alkaline solution of arsenobenzol in 150 to 250 c.c. of sterile physiological salt solution is injected directly into a vein. It is absolutely essential that this be done aseptically, and with perfect technique, in order to avoid serious complications. The solution used must be *absolutely clear*, otherwise alarming symptoms of collapse may develop. The injections are usually followed by some fever, nausea, vomiting, and occasionally a chill, but these symptoms usually subside in a short time. The injection properly given is practically painless.

The *intramuscular and subcutaneous injections* are given either in a neutral suspension of the drug, or else in a clearer alkaline solution. There is still some difference of opinion as to the comparative effects of this method, although Ehrlich prefers the alkaline solution injected into the muscles as being more effective. The neutral suspension is less painful than the alkaline solution. The subcutaneous method has the advantage that the depot of deposited arsenic is more surgically accessible in the event that a necrosis of tissue takes place. In the intramuscular and subcutaneous injections the amount of fluid employed is usually from 8 to 15 c.c. Recently some clinicians have advocated the use of arsenobenzol rubbed up in sterilized oil or in a thin unguentous base. It is too early to state the relative value of this method of preparation.

GENERAL RESULTS. The immediate effect of the use of arsenobenzol upon syphilitic manifestations is, in the vast majority of cases, marvellous. There is no other chronic infectious disease in which long-standing lesions can be influenced with such magic

rapidity.   Of course, it must be remembered that many syphilitic lesions respond in a most prompt and satisfactory manner to the influence of large doses of mercury, particularly when given by injection or inunction.   But these results are overshadowed by those observed after the new treatment.   Both early and late manifestations of syphilis are, as a rule, quickly influenced by injection of the Ehrlich preparation.

There are some cases, however, that respond only partially or not at all to the first injection, and require a second and even a third.   It would seem that the arsenobenzol destroys the spirochetes when it comes in contact with them.   It is likely, however, that in some lesions the vascular approach is cut off, and the drug is at least for a time unable to reach the parasitic organisms.

At the present writing it would appear that the hope of Ehrlich of achieving a *therapia sterilisans magna*—a cure at one stroke— will not be generally realized.   If future observation demonstrates that syphilis can be radically cured with Ehrlich's treatment, it will probably require at least several injections to effect the desired result.

This of itself would be a consummation most devoutly to be wished.   There is reason to believe that many cases treated by the usual methods in the past, and believed to be cured on clinical evidence, have in reality not been cured.   The persistence of the positive Wassermann test and the finding of spirochetes in visceral lesions many years after infection indicate that the mere effacement of cutaneous and mucous membrane manifestations is no adequate guide as to the disappearance of the disease itself.

Recent researches tend to show that syphilis plays a large part in the determination not only of grave nervous diseases, but also in degenerative changes in the bloodvessels, heart, kidneys, and other organs.   The extent to which syphilis contributes indirectly to the mortality of the race is a matter still open for further study.

No one is at the present time in a position to affirm or deny that the new Ehrlich treatment cures syphilis.   Sufficient time has not elapsed to determine whether those cases in which the clinical symptoms have disappeared, and the Wassermann reaction has

become negative, are definitely cured of the disease. The brilliant clinical results that have thus far been obtained, and the experimental work on lower animals, make us hopeful that with further perfection of methods, rapid cures may be achieved.

INDICATIONS. We are not quite prepared to assert that arsenobenzol should at the present time be used in all cases of syphilis. We should prefer to await the results of a longer period of observation. Treatment, however, is distinctly indicated in those cases of syphilis, which are refractory to other methods of treatment. Late lesions of the tongue and of the palms of the hands are often resistant to mercury. Such cases respond promptly to the Ehrlich prepa ation. As regards the treatment of early lues, it is justifiable with the consent of the patient to employ this treatment where no contraindications exist. The malignant and precocious cases of syphilis seem to do marvellously well under arsenobenzol, and frequently gain weight rapidly after its administration.

CONTRAINDICATIONS. The most important contraindications against the use of arsenobenzol are the existence of serious disease of the heart, particularly the myocardium, and of the bloodvessels. Inasmuch as arsenobenzol increases blood pressure, the drug should not be used in conditions in which bleeding is apt to take place, such as ulcer of the stomach, hemophilia, etc. In optic neuritis, the drug should not be employed, although in cases of luetic origin the treatment has been given with alleged good results. In diseases of the kidneys, apart from syphilitic nephritis it would appear risky to employ this therapeutic procedure. Ehrlich specially counsels against the use of arsenobenzol in advanced degenerative conditions of the nervous system, such as long-standing cases of tabes dorsalis and paresis. He states that twelve deaths have occurred in such cases. There would also appear to be danger in using arsenobenzol in cases of syphilis of the nervous system involving vital centres, for the reaction produced in the immediate neighborhood of the disease focus might determine a fatal termination. It is likewise inadvisable to employ this treatment in debilitated, anemic, and cachectic subjects, where this condition is not the result of syphilis.

WASSERMANN REACTION. The results published by various observers concerning the effect of the arsenobenzol treatment upon the Wassermann reaction have been most discordant. Schreiber and Hoppe state that in 84.6 per cent. of 150 cases the Wassermann reaction became negative in fifty days. Wechselmann reports that out of 268 cases treated with arsenobenzol 153 developed negative Wassermann reactions in four to five weeks.

On the other hand, Zieler's cases, observed as long as ten to fifteen weeks, did not show permanent negative reactions. Neisser reports 44 per cent. negative reactions between twenty and thirty days. Geronne stated that 60 per cent. of his cases became negative. He also observed 4 cases of primary syphilis over periods of five and six months that remained clinically and serologically well.

In a recent communication, Lesser reported that after alkaline intramuscular injections in 300 cases, the Wassermann reaction became negative in more than one-half of the men in thirty-two days, but only in a few of the women.

DOSE. The early dose of arsenobenzol employed was about 0.3 gram. This was found to be insufficient, and the dose has been gradually increased. Some clinicians have given as high as a gram and more without injurious effect. It is not proved, however, that the very high dosage is more effective than moderate doses. Zieler says that he has not received the impression that doses over 0.7 gram work better than those of 0.4 and 0.6 gram. The commercial product which has been placed on the market under the trade name of "Salvarsan" is dispensed in vials containing 0.6 gram, which may be regarded as the average dose for subcutaneous and intragluteal injections. For intravenous injections, the average dose is about 0.4 gram. Some clinicians gauge the dose according to the body weight, giving from 0.005 to 0.014 gram per kilogram. The last word on the question of dosage has not yet been pronounced.

I. CASES TREATED BY SUBCUTANEOUS INJECTIONS.

CASE I.—D. B., female, colored, aged twenty-four years. Numerous hypertrophic condylomata about vulva and great swelling of the genitalia; sparse papulosquamous eruption on trunk and extremities, palms, and soles. Patient was injected intragluteally with 0.4 gram of arsenobenzol on October 10, 1910 (a little of the fluid was lost). Within forty-eight hours the raised, moist papules had almost melted down to the level of the skin. By October 21 the condylomata had disappeared, and the great swelling of the vulva had entirely subsided. Within eleven days after the injection the palmar papules had disappeared, leaving desquamating excavations. The lesions on the cutaneous surface elsewhere improved considerably, but did not disappear. On November 26 evidence of relapsing lesions was present. There was a mucous patch on the lip, a papule upon the vulva, and a pronounced papulosquamous eruption on the soles of the feet with some lesions elsewhere on the skin. The Wassermann test was three units positive. On December 1, 0.8 gram of "606" was injected subcutaneously. There was but moderate pain and no toxic arsenical symptoms. The plantar and other lesions present underwent rapid improvement, and on January 3, 1911, the date of the last examination, the patient was free of symptoms of the disease, and was feeling very well.

WASSERMANN REACTIONS.

October 24, 1910	+ 2	units syphilitic antibody
October 30, 1910	+ $\frac{1}{2}$	unit syphilitic antibody
November 22, 1910	+ $1\frac{1}{2}$	units syphilitic antibody
November 30, 1910	+ + + $2\frac{1}{2}$	units syphilitic antibody
December 7, 1910	+ + + $2\frac{1}{2}$	units syphilitic antibody

CASE II.—X. Y., aged thirty-one years. In 1905 contracted syphilis, for which he states he took steady treatment. In 1906 large ulcers on legs, the pigmented scars of which are still visible. Married in June, 1908, wife and child healthy. In August, 1908, developed an abscess (probably a gumma) in posterior pharyngeal wall. After incision this discharged for eight months, finally healing under potassium iodide. In October, 1910, complained of pain between shoulder-blades, which was much worse at night. He gradually became worse and had a feeling of constriction about the chest. Patient kept at work until October 24, when pain became severe, and was accompanied by numbness and weakness in his legs. On November 4, 1910, he suddenly became completely paralyzed in both legs, lumbar and abdominal muscles, and was unable to maintain even a sitting posture. Incontinence of feces and urine

Reflexes at first exaggerated, later lost. Sensation impaired. Bed sores developed rapidly during the first weeks of confinement to bed. Temperature from October 24 to November 21, 100° to 101° F. Since the onset of the paralytic symptoms, patient had been given thirty to forty drops of a saturated solution of potassium iodide and $\frac{1}{15}$ grain bichloride of mercury, four times a day without any improvement.

On November 21, 1910 the patient was given subcutaneously an injection in the back of 0.45 gram of arsenobenzol in a neutral suspension. Experienced no pain. The iodide was continued. On the following day the evening temperature for the first time dropped to 99° F., and after two days became normal. November 24 to December 1, general condition improving; bed sores healing. December 1 to 10, returning power in lumbar and abdominal muscles, slight control of sphincters. From this time on the patient progressively improved. He regained control over his bowels and bladder, the patellar reflexes returned; he was able to move his legs and sit up in a chair. By December 29 he was able to stand and has gained weight. When last heard from he was walking about on crutches.

Case III.—E. R., aged twenty-eight years. Initial lesion three months ago. At the present time has a macular eruption on the forehead, legs, scrotum, and a marked palmar eruption. Mucus patches in throat. Wassermann and Noguchi reactions positive.

On November 3, 1910, 0.6 gram of arsenobenzol was injected in a neutral suspension beneath the left shoulder-blade. (Owing to an accident to the syringe, about $\frac{1}{4}$ of the quantity was lost.) Patient had severe pain at site of injection, lasting for several days. There was slight elevation of temperature and pulse rate.

The eruptive manifestations improved to an extent but never disappeared; later new mucus patches developed in the mouth.

Wassermann Reactions.

September 6, 1910	Reaction negative
October 6, 1910	Reaction positive +
October 14, 1910	Reaction positive + +
October 28, 1910 (after some Hg treatment)	Reaction positive, faint, less than 1 unit
November 7, 1910	Reaction positive
November 14, 1910	Reaction positive
November 25, 1910	Reaction positive 2 units
November 30, 1910	Reaction positive + + +

Case IV.—X. Y., physician, aged thirty-five years. Contracted syphilis in 1895, and was treated for three years. Alcoholic excesses. In 1908 severe headaches, worse at night; dilatation of left pupil and mild grade optic neuritis in left eye. In September, 1908, patient was found dazed and incapable of expressing himself, apparently due to a sensory

aphasia. Dazed condition lasted for three weeks; was placed on active mercurial treatment and iodides, with excellent results. Six months later developed convulsive seizures, which were followed by a protracted semicomatose state; head and eyes turned to the right during convulsions. Occurred at first once in four months, but increasing in frequency to once in three or four weeks. Under mercury and the iodides, the patient improved.

Wassermann reaction negative; Noguchi, weak positive; butyric acid, positive.

On October 25, 1910, patient received subcutaneous injection of 0.45 gram of arsenobenzol in neutral suspension. Practically no pain.

On October 14, 1910, the Wassermann reaction was positive. The patient and his physician think that his speech and mental concentration have improved. His headaches have disappeared.

December 24, 1910, patient had a mild convulsion lasting a minute or two.

January 6, 1911, Wassermann reaction negative.

January 13, 1911, patient has had no further convulsive seizures.

CASE V.—X. Y., male, aged sixty-nine years. Case of arrested tabes dorsalis. For thirty years a sufferer from severe and unremitting lancinating pains in legs and other parts of body, and absent reflexes. Eyes normal. Patient has been seen by distinguished neurologists here and abroad.

On November 19, 1910, was given 0.45 gram of "606" in suspension beneath the left shoulder-blade. Patient suffered a great deal of pain for several days. No improvement in lancinating pains.

CASE VI.—J. D., male, aged thirty-six years. Has an extensive papular syphilide of the follicular type on the trunk and extremities with a sparse eruption on the face. Remains of a chancre near the meatus urinarius.

On October 21, 1910, 0.5 gram of arsenobenzol was injected subcutaneously into the back. Moderate pain. (About a tenth of the fluid lost.) In the course of the following week the eruption paled considerably and many of the lesions disappeared. On November 26, 1910, the eruption still persisted although much improved. Wassermann test, two units positive $+$ $+$. As the patient was obviously not cured, he was then placed on mercurial treatment.

WASSERMANN REACTIONS.

October 21, 1910	Positive, 3 units of syphilitic antibody.
October 24, 1910	Positive, $1\frac{1}{2}$ units of syphilitic antibody.
November 22, 1910	Positive, 2 units of syphilitic antibody.
December 7, 1910	Positive, 2 units of syphilitic antibody.

Case VII.—G. E., female, aged twenty-nine years, infected by her husband during summer of 1910. When she first presented herself on November 10, 1910, she had a maculosquamous eruption on the face and a widespread macular and small papular eruption upon the trunk which had existed for three months. Persistent headache, worse at night. Wassermann reaction $+ + +$; Noguchi $+ + + +$ (November 11, 1910).

Patient was on November 11, 1910, given a subcutaneous injection of 0.45 gram of arsenobenzol in neutral suspension. Moderate pain for one day. On the following day the patient said that the headaches which she had had continuously for three months had disappeared and also the "misty vision" (of which she had not previously spoken) was greatly improved. Within seventy-two hours the eruption disappeared from the face and was paler on the body. November 22, 1910, Wassermann reaction $+$ faint: Noguchi $+$.

On November 29 the headaches began to recur. After an absence of two weeks, the patient presented herself on December 28: the eruption had disappeared, but she complained of constant severe headaches, vertigo, vomiting, and loss of vision in the right eye, with some dimness in the left. For a number of days she vomited everything she ate. She was sent to a hospital, where she was examined by Dr. George E. de Schweinitz, who reported that she had a choked disk with retinal hemorrhage, and almost no vision in the right eye, and beginning involvement of the left. He stated that the cause was intracranial pressure from a gumma or similar lesion.

Under the use of mercurial inunctions and 100 grains of potassium iodide a day ordered by Dr. Howard Hansell, into whose service she later came, her vision was improving when last heard from.

Case VIII.—S. B., female, aged twenty-three years. Infected with lues about two years ago. Has been under my observation and treatment since July, 1910. During the period of her treatment she received a course of inunctions followed by steady internal treatment. In September, 1910, she developed an ulcerating syphilide of the cutaneous border of the lip which spread at first slowly and later rapidly. Despite internal treatment and injections of gray oil (30 per cent.) varying in dosage, between 5 and 8 minims given between November 16 and December 5, the destruction of lip progressed until more than one-half of the lip was involved in the destructive process. Recognizing that some more heroic treatment was necessary to prevent the loss of the patient's lip, she was injected subcutaneously on December 6, 1910, with 0.5 gram of arsenobenzol. Within forty-eight hours the spread of the process had ceased, and the ulcer showed evidence of beginning granulation. The improvement progressed rapidly, and by December 24 the ulcerated area was entirely healed. No other treatment was used.

This patient had no pain after the injection, although she was an excessively nervous and apprehensive woman. The general condition of the patient was much improved after the arsenobenzol treatment.

II. CASES TREATED WITH INTRAVENOUS INJECTIONS.

The following cases were treated by injections of arsenobenzol ("606" of Ehrlich and Hata) given intravenously, following the prescribed methods of Schrieber, Weintraud, and Alt, and in some instances, intravenous injection was supplemented by subcutaneous injections. In one patient the injection was both intravenous and intramuscular.

In the preparation of the drug for intravenous injection the arsenobenzol was dissolved in sterile salt solution. The acidity of the solution was neutralized by the addition of proper quantities of a normal sodium hydroxide solution, and the total quantity for introduction into the vein was raised to 200 cubic centimeters by the addition of warm salt solution.

CASE I.—T. N., male, aged forty-two years. Initial lesion; genital chancre twenty years ago. History of early treatment indefinite, but the patient was apparently cured of the active manifestations of the disease.

In November of 1909, twenty years following the initial infection, the patient showed incipient symptoms of paresis. He was able to perform his business duties until April, 1910. The Wassermann reaction was strongly positive.

On October 18, 1910, the patient was treated by the injection of 0.4 of a gram of "606," one-half administered intravenously and one-half subcutaneously, employing the loose tissues about the scapula. Following the injection for a period of forty-eight hours, the temperature ranged from $98\frac{2}{5}°$ to $100\frac{2}{5}°$ F. There was a good deal of discomfort at the site of the injection, with some induration and tenderness.

At the present writing, the patient—having since received a second injection of arsenobenzol by another physician—shows no improvement or arrest of the disease. His delusions are more marked and his condition is absolutely hopeless.

CASE II.—T. G., male, aged forty-six years, denied all history of lues. The patient upon examination presented a perforation of the cartilaginous septum of the nose, having all the appearances of a healed syphilitic

ulcer. The Wassermann reaction was strongly positive, plus four. The diagnosis of paresis was made in October, 1909. At the time of the injection the patient was somewhat emotional and slightly delirious, with well-marked early symptoms of paresis.

On October 18, $\frac{4}{10}$ gram of arsenobenzol was injected, one-half intravenously, one-half subcutaneously, employing the loose tissues about the scapula. Following the injection the patient suffered considerable pain at the site of the subcutaneous puncture, some edema, swelling of the arm, induration marked, necessitating the application of ice bags for relief. A slough subsequently developed at the site of the subcutaneous injection. The temperature following the injection fluctuated from 100° to 102° during the next forty-eight hours, with nausea and some vomiting several hours after the injection.

At the present writing, the patient has left the institution, is without an attendant, and his disease apparently is arrested, judging from his ability to care for himself and save others from all annoyance.

CASE III.—J. B., male, aged twenty-five years. On September 7, 1910, multiple (two) chancres of the corona of the penis appeared at the usual time after exposure. At the proper time, secondary rash appeared, with adenopathy and marked injection of the soft palate.

He was not treated with any form of medication. Wassermann reaction was strongly positive.

On November 1, 1910, $\frac{5}{10}$ gram of arsenobenzol was given intravenously, employing the median basilic vein at the elbow. During the next twenty-four hours, following the injection, the temperature rose to 102°, accompanied by nausea and vomiting on the evening following the injection. At the end of twenty-four hours the patient was normal in every respect and was able to leave the hospital. The initial lesions cleared up completely in twelve days, and fourteen days later the cutaneous rash had entirely disappeared.

On January 10, 1911, according to the statement of his physician, he is suffering from a recurrence of the cutaneous rash.

CASE IV.—R. J., male, aged forty-two years. In December, 1908, had initial genital lesion. He was treated for two years without interruption by a well-known syphilographer in New York.

On seeing him in October, the patient had a small pharyngeal ulcer, a painful cervical gland under the jaw on the right side, and advanced arteriosclerosis. There was no other evidence of disease. Wassermann reaction strongly positive.

On November 1 he was given $\frac{4}{10}$ gram of arsenobenzol intravenously. During the following twenty-four hours he only suffered a rise of temperature to 99°. November 7 the mucous patch had completely disappeared, and there was no further evidence of ulceration about the mucous sur-

faces of the mouth, palate, or pharynx. A Wassermann was done again, because the patient was compelled to leave the city. It was found to be positive, but less marked than before the injection.

CASE V.—E. C. N., male, aged thirty-two years. June 1, 1910, initial genital lesion. Expiration of the usual period followed by marked generalized cutaneous syphilitic rash. The patient was an alcoholic. He was treated by a reputable physician, but failed to abstain from alcohol and take his medication regularly. He therefore relapsed and developed a pustular syphilitic rash involving all parts of the body, but most marked on the forehead at the hair line and on the wrist surfaces.

Examination of the mouth revealed a syphilitic ulceration involving the soft palate completely, both tonsils, and anterior palatine arches. The patient had lost a good deal of weight, and was running a temperature of 101°. The case was almost one of malignant type.

The patient received $\frac{5}{10}$ gram of arsenobenzol intravenously, and subcutaneously in divided amounts. Thirty minutes after the injection the temperature dropped to 97°, cyanosis became marked, the patient complained of precordial distress; nausea and vomiting developed, accompanied by diarrhea. There was apparently inhibition of respiration and cardiac embarrassment. He was stimulated with strychnine and hot water bottles, and slowly recovered from his collapse. He stated that he received the most comfort when lying on his abdomen during the attack, which lasted about an hour. At the end of twenty-four hours his temperature was 100°, and during the next four days the temperature fluctuated between normal and 101°.

He was exhibited four days later by Dr. George Fetterolf, who examined his throat—before treatment was instituted—before the Laryngological Section of the Philadelphia College of Physicians, and at this time his throat showed only a small patch involving the left anterior palatine arch. At the end of a week the mucous patch in his mouth had completely disappeared; and seventeen days after the injection, when last seen by the writer, his rash had almost totally disappeared. The patient had gained ten pounds in weight and felt decidedly better. He disappeared from view, having left the city, and has not been observed since.

CASE VI.—W. W. W., male, aged twenty-five years. Initial lesion early in 1910, followed by a secondary eruption after the lapse of the usual period, following the development of the primary lesion.

He was treated by his physician with large doses of mercurials, and apparently recovered from his secondary eruption, with the exception of an oral mucous patch which failed to disappear. No Wassermann was taken.

The patient was given $\frac{4}{10}$ gram of arsenobenzol intravenously, and one

week later the mucous patch had disappeared.   There was no reaction
to the injection of the drug.

CASE VII.—O. E., male, aged forty-two years.   Initial genital lesion
twenty years ago.

The patient had been a German soldier and was treated for a few
months with the prompt disappearance of his lesions.

When observed in September, he had a large gummatous ulcer of the
lower tibial region of the left leg involving the surfaces as extensively
as the palm of one's hand. No Wassermann. Following the intravenous
injection the patient developed no reaction to the drug. During the next
week an improvement was noted in the ulceration of the leg, and three
weeks later when exhibited before a local medical society there was
almost complete healing of the ulcer. At the present time, some three
months following the injection, the patient is clinically well.

CASE VIII.—A. S., male, aged thirty-four years.   Initial genital
lesion seven years ago, followed by the development of secondary erup-
tion. He was actively treated by his physician with huge doses of mer-
cury, supplemented with iodides in the treatment of the disease. The
disease was apparently arrested, with the exception of an oropharyngeal
ulcer about the size of a dime, which failed to heal under any form of
administration of mercury. The patient followed his instructions care-
fully, observing all precautions, and in no sense was negligent.

On November 7, $\frac{4}{10}$ gram of arsenobenzol was injected intravenously,
preceded by venesection. During the first twenty-four hours following
the injection the temperature rose to 101°, accompanied by some nausea.
No other discomfort was observed. One week following the injection
the pharyngeal lesion had completely disappeared, and at the present
writing there is no recurrence.

CASE IX.—R. B., female, aged twenty-three years; unmarried.   In
January, 1910, extragenital labial chancre was innocently contracted.
By contact, both lips were involved in the initial lesion.

When seen on November 1 the patient had a desquamative maculo-
papular rash, most marked at the hairline of the forehead, the alæ of
the nose, and the external auditory canals of both ears. There was also
some cutaneous manifestations of the disease over the anterior surface
of the chest. The Wassermann reaction was strongly positive; $\frac{4}{10}$ gram
of arsenobenzol was injected intravenously on November 10, 1910.
During the next twenty-four hours the temperature rose to 101°,
accompanied by nausea and vomiting, neither of which was marked.
At the end of ten days the rash had completely disappeared, and at
the present writing the patient shows some suspicion of recurrence on the
surfaces of the forehead and the forearms. There is some doubt as to
whether this is a true rash, as the macules are indistinct.

CASE X.—L. L., male, aged twenty years. Two genital chancres at the frenum. Smears of these lesions, taken by Drs. Uhle and Mackinney, demonstrated the treponema pallidum on successive days. The Wassermann was negative.

The patient was given $\frac{2}{10}$ gram in an oil emulsion intramuscularly on November 18, 1910; the intravenous injection consisted of 150 c.c. of the solution. The intragluteal injection consisted of 8 c.c. of an emulsion of the drug in a sterile olive oil. This drug was administered by one of the writers and Drs. Uhle and Mackinney, to whom the writers are indebted for the patient.

About fifteen minutes after the injection the patient complained of light-headedness, faintness, and inability to breathe. He was nauseated and attempted to vomit, but did not succeed in doing so. The cyanosis suddenly became intense, with pupillary dilatation, and the skin became cold and clammy. He gasped: "I cannot breathe," and seemed to be in extremis. The pulse at the wrist was scarcely perceptible, and very irregular. He was unable to speak, except to motion and draw attention to his intense suffocation. The case looked like one of sudden paralysis of the diaphragm, since all efforts at breathing were purely abdominal. Artificial respiration was at once employed, and $\frac{1}{30}$ grain of strychnine-sulphate was given hypodermically. Immediate percussion at the precordial area revealed no perceptible over-enlargement of the heart, such as Drs. Dorrance and Ginsburg had experienced in two cases of human blood transfusion. The heart sounds were muffled and almost inaudible. The patient was apparently conscious, but unable, owing to respiratory embarrassment, to articulate. Under heroic treatment the circulation improved, and the patient slowly recovered sufficiently to speak. At the end of two hours he had apparently become normal, and was able to be left unobserved.

In describing the onset of his condition, he stated that he felt as though "he had been kicked in the abdomen and lost his breath." The patient was very plethoric, and preceding the intravenous injection venesection was performed. The collapse in this case is not unlike that of Case V, except that the symptoms were more pronounced, and the patient had ceased to breathe and was only able to do so with assistance.

CASE XI.—S. S., male, aged thirty-five years. Genital lesion seven years ago; under continuous medical treatment since primary lesion.

The patient has suffered from beginning ocular tabes, and has been examined by Dr. de Schweinitz, who finds certain degenerative changes indicative of this form of tabes dorsalis.

On November 1, 1910, he received $\frac{4}{10}$ grain of arsenobenzol intravenously. This was not followed by the usual relaxation to the drug observed in the other cases. At the present writing, his physician states

that during the past two months there was apparently an arrest in the progress of the disease, but no improvement in his ocular condition.

Case XII.—Male, aged fifty-one years, infection seven years ago. More or less continuous treatment since. The patient has been a sufferer from a syphilitic glossitis, causing much pain and tenderness. Wassermann reaction positive. On January 4, 0.5 gram of salvarsan was injected intravenously. The injection was followed by nausea and some rise of temperature. The patient left the hospital after twenty-four hours. Since this time there has been a considerable relief of pain and tenderness in the tongue.

Case XIII.—Male, aged twenty-three years, infection in October, 1910, followed by secondaries and sore throat, which persisted up to the time of injection. Wassermann reaction positive. On January 7, 1911, 0.5 gram arsenobenzol was given intravenously. During the injection a little of the fluid leaked into the skin, causing sufficient pain afterward to require the use of morphine. The patient's physician reports that a week after the injection the rash had completely disappeared.

In this series of 13 cases, treated by intravenous injections, six of the patients presented either a primary lesion, a secondary eruption, or both, the infection dating back in no case longer than nine months. In all of these cases, the response to the drug was prompt and most satisfactory, the initial lesions disappearing and the cutaneous manifestations of the disease fading rapidly. The most striking results were observed in those patients with mucous membrane lesions in whom the improvement after the injection was almost magical in its rapidity, perceptible changes often taking place within twenty-four hours. In one case of paresis in which the treatment was administered merely experimentally, there was no arrest of the disease, and the patient failed to show any improvement. In a second case where the symptoms had been of long standing, the disease has apparently been arrested, since the patient is able to care for himself, and is living at his home without any observation save that of his physician. It is too early in this case to state whether the arrest is merely a remission, often observed in such cases, or whether it is a permanent improvement due to the treatment received.

The third case of parasyphilitic disease, one of ocular tabes, shows an arrest in the progress of the disease, which may likewise be only temporary, and which time alone will determine. In

one patient, who twenty years after infection developed a gummatous ulcer, which at the time of treatment had been of long standing, the response was slow but certain; and though it appeared that the dosage of the drug was a trifle insufficient, complete healing finally occurred.

RECAPITULATION. Twenty-one cases of syphilis treated with arsenobenzol; 8 subcutaneously and 13 intravenously.

Of the cases of secondary syphilis treated subcutaneously, one was freed of eruptive manifestations by two injections. In one the eruption has disappeared, but the disease is obviously not cured, as the patient has evidence of intracranial disease. In two cases the treatment failed to effect a disappearance of the existing eruption, possibly owing to insufficient dosage.

One case of late ulcerating syphilide of lip, lesion cured.

One case of tabes, not improved.

One case of cerebral syphilis, result indeterminable at present time.

One case of spinal syphilis, rapid improvement.

Of the *intravenous injections.* One case of paresis, not improved.

One case of paresis, improved.

One case of tabes, alleged improvement by physician.

One case of secondaries, free of symptoms for sixty days, later a recurrence of the eruption.

One case of secondaries, suspicion of recurrence after forty days.

One case of secondaries recently treated, free of symptoms at the end of a week.

One case of semimalignant late secondaries, free of symptoms when last seen.

Three cases of late secondaries, persistent mouth lesions, healed.

One case of syphilitic glossitis, rapidly improved.

One gummatous ulcer of leg, lesion healed.

One case initial lesion, healed to date. Subsequent Wassermann reactions negative.

CONCLUSIONS. In our experience the intravenous injections have produced a prompter response to treatment, and have exerted a more permanent beneficial effect than the subcutaneous administrations. This is in accord with the reports of Schreiber, Weintraud, and Alt, who distinctly prefer this method of introducing

the drug. Ehrlich has likewise come out in favor of intravenous injections because of their greater efficacy. All of the later 13 cases reported in this paper received the drug intravenously; in a few instances, the intravenous method was combined with the subcutaneous administration of the drug.

In only one of the cases where the intravenous method was used was there any pain at the site of the injection, and in this case it was due to an accidental leakage of the fluid beneath the skin. In neither the intravenous or subcutaneous treatments have we noted any instance of deep necrosis.

It is important in preparing intravenous solutions to avoid a fine suspension of the drug. This may be caused by the addition of too little sodium hydrate solution or by the use of salt solution made with commercial salt and undistilled water. It is highly important to employ a *completely clear solution*, which is obtainable by accurate neutralization of the primarily acid solution with sodium hydrate. Accompanying each ampoule of "Salvarsan" is a circular giving a graduated table of the precise amount of a 15 per cent. solution of sodium hydrate necessary to neutralize the various doses of the drug which are employed. It is wise, however, to add the alkali drop by drop, and test with litmus paper. It is best to use 150 to 250 c.c. of solution for intravenous injections, employing a physiological saline solution as the diluent. It is a good plan to first inject a little saline solution in order to be sure that the needle is in the vein. Patients receiving intravenous injections should be in a hospital where they can be kept under careful observation for at least several days following the treatment.

We desire to express our indebtedness to Dr. E. Corson White and Dr. John L. Laird for the Wassermann tests made on the patients referred to in this report.

REPORT OF LEON A. RYAN, M.D.

Professor Fischer and J. Hoppe[1] determined that the greatest part of the arsenic of the dioxydiamidoarsenobenzol is given off

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[1] Münchener med. Wochenschrift, 1910, No. 29.

by the urine, and relatively only a small part by the feces. Greven[1] has published investigations bearing upon the beginning of the arsenic elimination by the urine, and the length of time of its continuance in the urine after the injection subcutaneously and intramuscularly of doses ranging between 0.35 gram and 0.6 gram of the compound in fifteen men, aged between fifteen and thirty years, affected with lues. The method employed by Greven for the qualitative detection of the arsenic in the urine was the biological method of Gosio (with the Penicillium brevicaule mould). Greven found that the beginning of the elimination of arsenic in the urine ranged from twenty-five minutes to sixty minutes after the injection and continued in the urine for periods ranging from fourteen days to twenty-five days. No quantitative determinations were made by Greven. The results given in this article state the amounts of arsenic found by us in each twenty-four hours' urine of two patients running over a period of three consecutive days in each case.

All of the chemical reagents used in the experiment had been previously tested, and found to be free from arsenic.

For convenience the patients will be designated by the numbers 1 and 2. Patient No. 1 received a dose of 0.8 gram of dioxydiamidoarsenobenzol, and patient No. 2 received a dose of 0.5 gram of dioxydiamidoarsenobenzol.

Each twenty-four hours' urine was treated identically as follows: The twenty-four hours' urine passed by each patient was strongly acidulated with concentrated nitric acid, and evaporated to a thick syrup on a water bath. The residue thus obtained was treated with concentrated sulphuric acid, and heated on a sand bath until apparent carbonization of the organic matter was effected. The charred mass was then slightly acidulated with nitric acid, and extracted with repeated portions of hot distilled water. The solution was then filtered, and the filtrate evaporated to dryness on a water bath, and whatever organic matter remained was carbonized with concentrated sulphuric acid, and the residue was extracted with hot distilled water acidulated with a few drops

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[1] Münchener med. Wochenschrift, 1910, No. 40.

of hydrochloric acid, and the filtrate concentrated to a small volume. The arsenic was then reduced by boiling the solution with a few drops of strong sulphurous acid. Washed hydrogen sulphide was conducted through the solution for several hours, and the liquid allowed to stand over night, and again treated with hydrogen sulphide and then warmed until free from odor of hydrogen sulphide. The resulting sulphide of arsenic was collected on a hardened filter paper, washed with hydrogen sulphide water and then with distilled water until free from chlorine, and finally dissolved from the filter paper with dilute ammonium hydroxide (1 to 9). The ammoniacal solution was collected in a small glass dish, and evaporated to dryness on a water bath. The residue was repeatedly treated with a few drops of concentrated nitric acid, and after each treatment evaporated to dryness on a water bath. The residue was again re-dissolved with hot distilled water, concentrated to a small volume, and the arsenic reduced to the arsenous condition with sulphurous acid. The arsenic was then re-precipitated with washed hydrogen sulphide. The resulting sulphide of arsenic was collected on a hardened filter paper, washed with hydrogen sulphide water and finally with hot distilled water until free from chlorine. The sulphide of arsenic was then dissolved from the filter paper with dilute ammonium hydroxide (1 to 9) and the ammoniacal solution was collected in a weighed glass evaporating dish. The ammoniacal solution was evaporated to dryness on a water bath and placed in a desiccator over concentrated sulphuric acid. To remove any possible adherent sulphur the sulphide of arsenic residue was carefully washed by decantation with redistilled carbon disulphide and again placed in desiccator and finally weighed.

To substantiate the arsenical composition of the precipitate, each precipitate weighed as sulphide of arsenic was evaporated twice to dryness on a water bath with strong nitric acid, and the residue was dissolved in a small volume of distilled water. These aqueous solutions responded to the characteristic silver nitrate and copper sulphide tests for arsenic acid.

Patient No. 1. December 2, 1910. Volume of twenty-four hours' urine, 870 c.c.; specific gravity, 1016; alkaline in reaction;

yielded 0.0018 gram of arsenous oxide or to 0.00109 gram metallic arsenic.

Patient No. 1. December 3, 1910. Volume of second twenty-four hours' urine, 1060 c.c.; specific gravity, 1020; alkaline in reaction; yielded 0.0038 gram of arsenous sulphide, equivalent to 0.00305 gram of arsenous oxide or to 0.0023 gram metallic arsenic.

Patient No. 1. December 4, 1910. Volume of third twenty-four hours' urine, 650 c.c.; specific gravity, 1020; alkaline in reaction; yielded 0.0026 gram of arsenous sulphide, equivalent to 0.00209 of arsenous oxide or to 0.00158 gram metallic arsenic.

Patient No. 2. December 6, 1910. Volume of urine, 720 c.c.; specific gravity, 1020; acid in reaction; yielded 0.0029 gram of arsenous sulphide, equivalent to 0.0023 gram of arsenous oxide or to 0.00176 gram metallic arsenic.

Patient No. 2. December 7, 1910. Volume of twenty-four hours' urine, 790 c.c.; specific gravity, 1024; acid in reaction; yielded 0.0036 gram of arsenous sulphide, equivalent to 0.0289 gram of arsenous oxide or to 0.00219 gram metallic arsenic.

Patient No 2. December 8, 1910. Volume of urine, 2000 c.c.; specific gravity, 1018; acid in reaction; yielded 0.003 gram of arsenous sulphide equivalent to 0.00241 gram of arsenous oxide or to 0.00182 gram metallic arsenic.

Patient.	Date.	Volume of urine.	Reaction.	Specific gravity.	Weight in gram of dioxy-diamidoarsenobenzol administered.	Weight in gram of As₂S₃ recovered.	Equivalent in gram of As₂O₃.	Equivalent in gram of As.	Equivalent in gram of dioxyamidoarsenobenzol.	Per cent. dioxyamido-arsenobenzol voided.
1	Dec. 2	870	Alkaline	1016	0.8	0.0018	0.00144	0.00109	0.003511	0.438
	Dec. 3	1060	Alkaline	1020		0.0038	0.00305	0.00230	0.007415	0.926
	Dec. 4	650	Alkaline	1020		0.0026	0.00209	0.00158	0.005089	0.636
2	Dec. 6	720	Acid	1020	0.5	0.0029	0.00230	0.00176	0.005669	0.708
	Dec. 7	790	Acid	1024		0.0036	0.00289	0.00219	0.007054	0.881
	Dec. 8	2000	Acid	1018		0.0030	0.00241	0.00182	0.005863	0.732

DISCUSSION.

DR. FRANK CROZER KNOWLES: Practically all of the articles first written on the subject of "606" were a unit in the praise of Professor Ehrlich's preparation. The tide is now somewhat turning, and I would like to say a few words on the adverse side of the subject.

There are several almost insurmountable difficulties in the use of "salvarsan," excepting in selected cases, unless the technique can be simplified and the dangers lessened. First, the use of the drug should be preceded by not only careful examination of the organs and vascular system, but also of the inner structure of the eyes. Second, the preparation of the drug for injection requires, if the Wechselmann method is used, approximately one hour, and if the simpler technique of Lesser is employed, about one-half hour. Third, it is almost essential that cases treated by this drug should be kept in bed for several days, to prevent either serious discomfort or complications.

The remedy is, moreover, not infallible, as was at first thought; as an example, several cases may be mentioned in which the injection elicited no response; Hügel and Ruete reported three instances, Etner, Iversen, and Fordyce each one, and many more could be added. The literature is now filled with relapses following the use of this drug. In Hügel's series of 30 cases there were 4 which relapsed; Sieskind recorded 7 relapses in 35 patients; of the 16 cases treated by Nichols and Fordyce, 2 show a recurrence of the disease; of the 10 cases in which the drug was used by Varney, of Detroit, 3 have relapsed. Büschke, of the Virchow Hospital, Berlin, states that he will only use "salvarsan" in those cases in which mercury or the iodides have failed. Of 10 cases treated by Dr. Longcope, several of which were referred from the skin dispensary of the Pennsylvania Hospital, one has already relapsed.

Salvarsan is not the "therapia sterilisans magna" as was at first thought; it is an important aid in our treatment of syphilis, but will not, in my humble opinion, displace mercury in the cure of the disease.

DR. H. M. CHRISTIAN: My experience with "606" has been limited to about 7 cases only, owing to the inability to get the drug freely. The first case was injected at my request by Dr. Daland, and was a case of tertiary syphilis with a necrotic gummatous ulcer at the ankle of about two years' duration. The man had been taking the mixed treatment, mercury and potash, for over a year. Dr. Daland will remember the case very well. The patient was injected in the gluteal region about six weeks ago. An astonishing result followed the injection. The ulcer on the leg healed promptly within ten days and the man gained in weight from fifteen to eighteen pounds. The ulcer today is absolutely healed and the gain in weight has been maintained.

The next patient was a student, and a dose of the drug was secured through the courtesy of Dr. Anders. He had a chancre which had resisted all ordinary methods of treatment. He was put into the ward and given one dose of "606." The temperature ran to 103° to 104° for two nights and then dropped to normal. At the end of four days the chancre, which had resisted all previous treatment, took on healthy granulation, and in a week it was entirely healed. The osteocopic pains had gone and the mucous patch in the mouth had disappeared. Through the courtesy of Dr. Flexner we have been furnished at the Philadelphia Hospital with some of the drug. I have had five cases there. One case of acute roseola with sclerosis of a chancre was not much affected. In a case of papulosquamous eruption an injection was given last Friday, and the man is in a remarkable condition today. The eruption has almost entirely scaled off. In all these cases the Wassermann reaction was positive. One case of large papulosquamous syphilis is not much improved. The last case will be a test one for "606." This is a case that a year ago, when I went on duty at Blockley, was there with glossitis, which is admitted to be the most troublesome form of tertiary syphilis. I went off duty the first of April and left him in the ward. When I went on duty, the first of December, there was the same condition. He was given an injection two weeks ago, and with a large stretch of the imagination he could be regarded as somewhat better.

DR. S. SOLIS COHEN: A single case don't amount to much, but there is a peculiar psychic effect of "606," which may be noted concerning this one patient, whom you, Mr. President, were kind enough to examine for me at Blockley before the remedy was administered, to determine whether or not there were any eye lesions. A colored man, much emaciated, was admitted to the medical ward on account of enlarged liver. We found that there was a perforation of the palate extending through the bone as well as the mucous membrane, and a gumma in the neighborhood of the sternoclavicular articulation which was giving considerable pain. Through the courtesy of Dr. Coplin and Dr. Funk $\frac{8}{10}$ gram of the neutral solution was given by injection into the muscles of the back. The pain of the gumma, which had been excruciating, disappeared within a couple of days, and all other external evidence of disease disappeared. The Wassermann reaction, however, has remained continuously positive for some twelve weeks. The man feels well; his appetite has been good, and he has gained in weight. He became happy and "got religion," and there being no minister of his own kind at hand, he called upon the good offices of a priest and entered the Roman Catholic fold. He said he must express his gratitude in some way for the great benefit received.

A curious fact in connection with this case is that although daily and

careful examinations of the urine were made by the analysts connected with the Philadelphia Hospital, arsenic was never found in the urine. What became of the arsenic I do not know. The feces, unfortunately, were not examined.

DR. F. X. DERCUM: I would ask for a more definite expression by the readers of the papers as to dosage and method of administration. I think possibly that some of the differences in results could be explained by differences in dosage and method.

DR. DALAND, closes: It is very important to remember that now we are beginning to hear of relapses. There have been a large number of relapses reported in Berlin, and for this reason it has been decided definitely that the method of administration should be changed from the intramuscular to the intravenous. The intravenous dose for a male adult should be not less than 0.5 gram. More than one gram has been given intravenously without ill effect. It is well to follow the advice of Professor Ehrlich that the alkaline solution should be employed in all intramuscular injections. The point that Dr. Cohen made regarding the urine being arsenic free, I cannot explain. Most of the reports show that arsenic remains in the urine for from ten days to two weeks or longer, and has been found in the fecal discharges for about the same length of time. When given intravenously the arsenic is supposed to disappear from the urine in about four days, but recent observation at the Rockefeller Hospital shows that it persists much longer.

DR. SCHAMBERG closes: I was much perturbed in my case in which serious ocular symptoms developed until I had the reassuring opinion of Dr. de Schweinitz. Wechselmann states that he has used arsenobenzol in 1400 cases, and has observed no untoward effects as far as the eye is concerned. He furthermore states that in 20,000 cases now treated there is no indubitable record of injury to the eye, although several cases of alleged injury have been reported.

It must be remembered that syphilis is a very much more serious and persistent disease than we have been accustomed to think. In many of our cases, despite the effacement of skin and mucous membrane lesions and the absence of other discoverable manifestations, we still find positive Wassermann reactions. Pathological examinations within recent years have shown that in many syphilitic patients dead of other diseases spirochetes are found in arterial walls and other tissues. As Metchnikoff says, syphilis is not a fatal disease, but it takes high rank among conditions that bring about human mortality. The probability is that the spirochetes pass only once in large quantities through the blood current, and are deposited focally in the various tissues. Furthermore, it is probable that many of the spirochetes are walled off by occlusion of

bloodvessels and are not reached by the drugs administered. The invading hosts of spirochetes, like retreating armies, often burn the bridges behind them.

Regarding the value of the particular remedy under consideration, the attitude of satisfaction or of dissatisfaction with the results obtained must depend largely upon the point of view. Those who were led to expect a cure at one stroke doubtless experience a feeling of disappointment. Those, however, who recognize that we have had introduced into our therapeutic armamentarium a drug of marvellous immediate value cannot but feel that a great advance has been made. Doubtless many cases of syphilis will require a repetition of treatment by this drug. At the present time arsenobenzol has its chief indication in those cases which resist mercury and iodide. It is perhaps fortunate that there is a halt in the exuberant enthusiasm excited by Ehrlich's announcement, for this may retard injudicious haste in the use of the drug by unqualified persons and in conditions in which it should not be employed. At the present time, given a robust individual with early syphilis who desires this treatment, it seems to me that we are perfectly justified in using it.

CERTAIN ANGIONEUROTIC MANIFESTATIONS IN AND AROUND JOINTS, FREQUENTLY MISTAKEN FOR GOUT AND RHEUMATISM.[1]

ABSTRACT.

By SOLOMON SOLIS COHEN, M.D.

AMONG the less common, and even less commonly recognized, phenomena of recurrent angioneurotic crises are painful swellings in and around the joints. These may occur as the only symptoms, or may be associated with other persistent or paroxysmal vasomotor disturbances, or may be among the varieties of paroxysmal disorder occurring at various times in the subject of vasomotor ataxia.

One form of vasomotor joint disorder has attracted especial attention, and has received the designation of intermittent joint effusion, *hydrops articulorum intermittens*. It was apparently first observed by Perrin[2] (1845), then by Moore[3] (1852, 1865), and others. Fridenberg[4] was the first American reporter, and Schlesinger[5] has made the most complete study of the condition. This form of the affection is usually periodical in its manifestations, and is rarely associated with febrile movement. Hence, although it is in many cases at first mistaken for acute articular rheumatism, its true nature soon becomes apparent. The effusion in these cases commonly takes place within the capsule (or the

[1] Read January 4, 1911.

[2] Jour. de Méd. de Trousseau, 1845, p. 82; L'Union Méd., 1878, No. 61.

[3] Med.-Chir. Trans., London, 1867, ser. II, vol. xxxii, p. 19.

[4] Med. Rec., New York, 1888, p. 657.

[5] Mitt. a. d. Grens. d. Med. u. Chir. v. Jena, 1900, p. 441 et seq.; Nothnagel's System, 1903.

joint structures proper), and the knee is most commonly affected, although no articulation in the body seems to be exempt. Periarticular effusions, however, also occur, and are very frequently mistaken for rheumatism or gout. The involvement of soft parts in connection with hydrops articulorum has been recognized by Schlesinger and a few others, but so far as known to the writer, the isolated occurrence of these swellings has not been dwelt upon in the literature. Hence it may be supposed that their true nature is seldom recognized.

As a rule, they probably affect most frequently the smaller joints, especially the wrist and fingers, less commonly, perhaps, the toes, or the big toe; and, while sometimes periodical, they may be quite irregular in their recurrences. Both intra-articular and periarticular effusions may occur at the same time. The phenomenon is probably identical in mechanism with the more commonly recognized forms of angioneurotic edema, and the subjects, in so far as they have come under the writer's observation, exhibit the stigmata to which he has so frequently called attention.[1]   In reported cases, the frequent association of angioneurotic phenomena of various kinds, including both Graves' phenomena and Raynaud's phenomena, would indicate that the patients likewise belong to the same group of subjects; and that the distinguishing characteristics would have been found in most, if not all, of them had the examination been made.

Reported cases of intermittent hydrops articulorum have been divided into *essential* and *secondary*—the former occurring in healthy joints; the latter following, or being associated with, articular disease or injury. A further division into neurotic and non-neurotic cases has been suggested. Non-neurotic cases would not fall within the limits of this paper. The neurotic cases show the same predispositions in family and patient and the same groups of exciting and determining factors that the writer has pointed out for angioneuroses in general. Fatigue, emotion (especially anxiety and fear), toxemia and atmospheric changes are the principal known

[1] S. Solis Cohen, on Vasomotor Ataxia, Amer. Jour. Med. Sci., Feb. 1894; Trans. Assoc. Amer. Phys., 1902, p. 654 et seq. and 1909; N. Y. Med. Jour., Feb. 19, Feb. 26, Mar. 5, 1910.

excitants; mechanical causes are the principal local determinants demonstrable.   In many cases, however, neither excitant nor determinant can be recognized.

Six selected illustrative cases were reported; 2 of intra-articular, 4 of extra-articular swelling; 2 involved the knees; 2 the hand and wrist; 1 the big toe; 1 the lumbosacral articulation.   Five of the patients were women.   Reported cases, numbering about 80, show but a slight preponderance of females.

MODERNIZED VIEWS OF RABIES, WITH REPORT OF CASES.[1]

By LEONARD D. FRESCOLN, M.D.,

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It may be of interest now to review the subject of rabies, as the disease is rather rare with us, but cases are likely to be met and handled, especially in a large city hospital. The term *hydrophobia* is an old one, dating from the time of Celsus (first century B.C.). The disease was known vaguely as early as the fifth century B.C., in the time of the Laughing Philosopher, and in the time of Aristotle, fourth century B.C. Pliny speaks of the disease under the term λύττα (a worm), supposing that in dogs possessed with the malady there was a worm to be found under the tongue—in reality an enlarged frenum. Later, the Latin term *rabies* was used to denominate the affection, as it became known that fear of water, fear of oily substances, and fear of air (aërophobia) were merely manifestations of the highly irritable state. Emphasis upon this dread of taking water has come down through the ages.

> So bends tormented Tantalus to drink,
> While from his lips the refluent waters shrink.

There has been much discussion of hydrophobia ever since the patriarchal days of Xenophon and Plutarch. Great Britain, United States, Germany, France, Norway, Sweden, Belgium, and all civilized countries now recognize the disease, as do all the great veterinary schools in the world. Postmortem findings and

[1] Read October 4, 1911.

careful animal inoculation have done considerable to enlighten us as to the nature of the disease; moreover, the Pasteur treatment and health regulations, as we shall see presently, have done much to reduce human mortality. We must move cautiously, as the fear of this dread disease is liable to upset and discourage us in handling it at all. It has been termed the most dreadful of all diseases.

What primitive ideas are found in early medicine! Compare some of the theories and treatment, e. g., of this disease, described years ago, with the teaching and proofs of modern day medicine. In 1800, Ward, in speaking of the nature of hydrophobia, says the "proximate cause" of the disease is "retrograde activity of the faculties of the "sensorium." In more modern language this would not mean much; this much has been said, that it is "not a specific, inoculable disease." The bacillus of rabbit septicemia was at one time thought to be the cause. Virchow showed the fallacy of its spontaneous origin. Samuel Johnson, in speaking of the etiology, called it "a substance, nobody knows what," and here is about where we rest today on the question of its etiology.

It was once thought that hydrophobia occurred most frequently in the dog days—in the heat of summer, when the dog star was in the ascendancy. Statistics now show it to be most common in the spring and least common in the fall. It was once thought that a case could occur after as long a period as twenty years (according to Morgagni), or even thirty-eight years (according to another writer) after a bite. The incubation period is put down now as between ten days and one year—generally, however, within three months, and most commonly at about six weeks. In Venice the thought prevails that dogs develop hydrophobia because of thirst, and on this account shops must provide a little water trough before their doors. This is a good rule in hot weather to keep the animals in good condition. In Egypt the disease is unknown; in some of our States, California, e. g., it is rare at present; in Missouri and Ohio it is common; in Hamburg and Saxony it is common also. Its frequency in some localities has been modified, as we shall see, by modern treatment.

Saliva was proved by Magendie to be the infective agent in human beings. Galtier, of the Lyons Veterinary School, transmitted the disease to rabbits. In 1874 it was known that the disease was acquired only by saliva, generally of a carnivorous animal, coming into contact with a wound. As in many other infections, we find that the debilitated and alcoholic are in more danger of becoming a prey to the disease when exposed.

In hydrophobia, at postmortem examination there is to be found, in addition to congestion of the pharynx and internal organs in general—long ago noticed—a distinct congestion of the pons and medulla. In 1891 Babes found degeneration and a zone of embryonal cells in the medulla and pons. There is also degeneration of the intervertebral ganglia. These last two conditions are also to be found in chronic alcoholism, etc. The gross pathology of rabies is, for the most part, similar to that of uremia, septicemia, or delirium tremens. There is one case reported as having a ruptured pleura from the convulsions. Glycosuria may be found, especially in dogs affected with the disease.

Now, as to what is considered by the best authorities as almost pathognomonic of rabies, namely, the so-called Negri bodies. In 1903 Negri noticed degeneration of cortical nerve cells in rabies cases. The following is quoted from A. M. Stimson's very complete *U. S. Marine Hospital Bulletin*, recently published: "Negri has recently summed up his work upon the 'parasite of rabies'—*Neurocytes Hydrophobiæ Calkins*. He traces a developmental cycle for the organism, which he classifies with the sporozoa. The bodies consist of a groundwork of protoplasm, which contains ' inner bodies.' These latter are of two general types, with transitional forms between them. The types are: (1) Small, roundish, and highly refracting; (2) larger, less refracting, roundish, oval, or irregular. Both types are found in the same body. They are not artefacts, being found in unstained fresh tissues. . . . These bodies are very generally admitted to be very constant in rabies and peculiar to it."

These bodies are best found in Ammon's horn in the hippocampus major, from which smears should be made. The medulla

may be preserved in glycerin for future study. The following is mentioned as a good stain: The smears are put into Zenker's fluid, 15′, washed, placed in 95 per cent. alcohol tinted with iodine; absolute alcohol, 5′; 10 per cent. eosin, 5′; polychrome methylene blue, 3′; water; 95 per cent. alcohol. Sections may be hardened very readily in acetone, 45′, and run through several changes of paraffin. Omit the iodine-tinted alchool in staining these sections. Von Gieson's stain, or a modification used by S. B. Moon, will readily show these cell inclusions. Negri bodies, it is said by some, may be found also from a death agony.

Arnold, in 1792, in describing symptoms of rabies, laid stress upon the jumping of the heart and the cries of one patient, "Take him away, take him away." It has been noted already what emphasis was always put upon the fear of water, apart from the pain and excitement it causes. Among the most characteristic symptoms now noted are the irritability, the sensitiveness of the ear in responding to noise and setting up convulsions, spasm of the pharyngeal muscles in attempting to swallow, painful consciousness, and, later, paralysis.

In investigating a case suspicious of having been exposed to the possibilities of developing rabies, we now naturally strive to make an accurate investigation as to the dog in question. Did the dog have hydrophobia, and did the dog bite the patient? As early as 1812 it was enjoined that the animal be not killed at once. The dog should be watched closely at least two weeks, and, if showing no signs but merely has the history of having been exposed to the disease, it should be quarantined six months. A dog acquiring the disease will act peculiarly, will show unnatural affection for its master, pick up bits of paper, show some trouble with the mouth, have blood-stained vomitus, low barking, apathy toward other dogs, restlessness, seeking retirement, visual hallucinations. It will not pursue a person and try to borrow trouble. In addition to examining the dog's brain and cord, rabbit inoculations are often wise, death of the animal occurring in eight days. They are best inoculated subdurally after trephining, or by giving in salt solution in the muscles of the neck. In case of the death of the

patient and no autopsy permitted, the saliva or cerebrospinal fluid may be used with rabbits in order to try to determine a diagnosis.

Old superstitions created imaginary cures for many maladies. Lizards, herbs, and stones all have had their part to play in the pharmacopeia of the ancients. Hydrophobia, no less than other maladies, has been the subject of all sorts of speculation as to treatment. Modern preventive treatment of hydrophobia is proving more and more its usefulness. It has been found by conscientious laborers in the field of medicine that most is accomplished, especially in large problems, by those who tactfully approach the subject with forethought and good judgment. Pasteur realized this. Think of the opposition he met even so! But think also of the utter downfall that awaited him in the event of misdirected, overstrenuous efforts in the face of superstition and ignorance! He said on one occasion, "Mais avant la réalisation de cette espérance un long chemin reste à parcourir," and it is yet quite a road to the complete satisfaction of particularly the laity in the diagnosis and treatment of rabies.

Doctor Hunter stated that not a case had been helped in two thousand years. In reviewing old forms of treatment, we find that Galen administered a remedy for this disease. Cold water dashed on the head was a favorite procedure. A dog was said to have been cured by keeping it entirely under water, excepting the nose, for three days. This, by the way, is an early illustration of the use of the continuous bath. Ward, in 1809, advised the external application of opium; arsenic was used for a long time, also belladonna, entrails of insects (used in India), galvanism, snakestone, skull-cap leaves, mad stone (composed chiefly of calcium triphosphate), purging with magnesia and rhubarb, laudanum, olive oil, warm baths, musk, camphor liniment to the throat, ipecac in 10-grain doses, spirit of mindererus, steel, phosphorus (supposed to be destructive to the virus), salt water, excision, vinegar (in Germany), tree box, etc. These remedies have dwindled down in modern times to cauterization with fuming nitric acid, administration of chloral as sedative, biniodide

of mercury, and the early administration of the Pasteur preventive treatment is the only sheet anchor. Municipal and State laws have now accomplished much in prophylaxis against the disease.

After considerable experimentation on monkeys and then on dogs, it was found that the incubation period was lengthened from eleven to twenty-three days; then rabbits were used, and after passing the virus through ten rabbits, an eight-day period was reached. Heat was found to weaken the virus. The rabbits' cords are dried in bottles containing potassium hydrate at 22° C. About 1881, a rabbit injected with rabies virus developed the disease in fifteen days, and died in seventy-two hours; a second one developing the disease from the first, etc., through fifty rabbits, the incubation period was reduced to seven days. About 2.5 c.c. of salt solution and 0.5 cm. of cord are used for one injection. Upon this principle the virus is prepared for treating. Pasteur himself refers in his work to analogy to "cow pox" in the application of this principle.

Preventive administration of the virus is practised much more now than formerly. In 1895 eleven were given the treatment in Massachusetts, and in 1907, 165. It was found that with the Pasteur treatment the mortality of rabies had been reduced 10 per cent. (according to Marx) of what it used to be. Here is a recent clipping as to reduction of the mortality:

A continuous decrease in the number of cases of rabies in France is shown by the report of the Pasteur Institute of Paris. In the year 1886 there were treated at this institution 2671 persons, and of these 25 cases were fatal, probably because of delay in treatment. In 1896 the number of patients treated had fallen to 1308, with 4 of them fatal. Each subsequent year showed a steady decline in the number of patients, which totalled about 1000 in 1902. In 1908 and 1909 the number had fallen to 524 and 467 respectively, with a single fatal case in each year, and in 1910 the number of cases treated was 401, with a clean bill as far as mortality is concerned.

The inoculation is not a serious procedure for the preparing of the rabbits' cords, and in Paris at present it is done without the

use of ether. There is no necessity of causing even the least pain
to the lower animals in this work, and the result of the inocula-
tions is invaluable. As Keisle says, it were better to sacrifice the
whole breed of dogs in order to save one human life. Welsh has
well pointed out how many lives are now saved by Pasteur virus.
During an outbreak in 1899, in the District of Columbia, 21
were bitten; the Pasteur treatment was instituted, and not
one died. Hunter asserts that only about 5 per cent. of the cases
bitten end in madness. Wounds about the bare face and neck
are most deadly.

There is no authentic case of the fully developed disease that
has ever ended in recovery. The disease has been eradicated
from Denmark, Norway, Sweden, England (1897), and Switzer-
land. In Australia there exists a six months' quarantine for
newly arrived dogs. Restrictive measures on the part of the
government regarding dogs have helped to stamp out the disease
from parts that once had it: e. g., ownerless dogs are caught; if
rabies is near by, muzzling is enforced; dogs on the street must be
kept in leash; all cases of hydrophobia must be reported to the
board of health; imported dogs must be quarantined. Some dis-
tricts have all these measures to enforce, and some have only a
few.

Seldom does death result when preventive treatment has been
started early. Three out of 19,000 patients treated showed
paralysis, but lived. There may be pain at the site of injection,
a moderate temperature, and, as stated, recovery is the rule. For
an account of the labors of Pasteur, see the work, *Louis Pasteur:
His Life and Labors*, written by his son-in-law. Some interesting
cases have occurred in recent years, showing the worth of the
Pasteur treatment. We must, however, be alert and try to
ascertain just how much real worth resides in each treatment.
The affection pseudolyssa, or an hysterical syndrome somewhat
simulating the symptomatology of rabies, is occasionally met;
such an animal will sometimes bark and carry on in quite a strange
way. These cases can be diagnosticated, as a rule, but hysteria
may closely simulate the disease. I should think it would be a

difficult matter, however, for a pathologist to really understand in full the old conception of a person being "frightened to death."

There is on record the case of a physician helping in this work who developed the disease and finally refused treatment; he died about as soon as the inoculated animals. There was a policeman in Massachusetts who acquired the disease and ridiculed the idea of the treatment and refused it; he died, and a comrade, receiving a wound from his teeth, took the treatment and lived. It cannot be proved the second man would have developed the disease, but it is quite likely, judging from our familiarity with its transmission. Notwithstanding, a few physicians still question the existence of the disease or aver that of the cases called hydrophobia very few are genuine. The *Washington Post*, even in comparatively recent years, published the following: "Hydrophobia is the product of a diseased mind, stimulated by the vaporings of quacks and humbugs." Here is a quotation from one physician: "Pasteur's method hardly attracts any attention now, and seems to be in a fair way to die a natural death."

Kierle lays down the rule that if the case is even a suspicious one, institute the treatment. The treatment may be shipped each day, say for twenty-five days, as from the laboratory of the New York Board of Health, Sixteenth Street and river front, and the expense of making the virus (twenty-five dollars) is charged. The bottle should be kept on the ice until used that day. Some firms now send the virus in refrigerating carriers; this is more expensive. Patients may be sent to the nearest institute for treatment if they so desire and can afford to pay.

In handling a case do not alarm or disturb the patient any more than is necessary; keep the patient away from alcohol.

During the last few years the following notes were made on some patients under my observation. (Most cases quoted are of persons exposed to the disease):

Case I. —(Exposed.) A. B., admitted to Women's Medical Ward, November 26, 1909; white, aged forty-four years. Bitten by mad dog on both hands few days before admission. Examination of dog: Negri bodies positive. Two series of rabbits were inoculated from the dog, and

they died on about the eighth day. Report from the State Laboratory. Patient's wounds were immediately cauterized. Pasteur virus was administered as follows: 3 c.c., November 28 to December 1, inclusive. (November 29, 6 c.c. were given). December 2 to 13 inclusive, 2.5 c.c. were given. Patient was discharged December 13, 1909. Inquiry was made three months later, and she was found to be in good health.

CASE II.—(Exposed.)   A. N., white woman, aged thirty-eight years. Admitted June 14, 1910. Patient was bitten May 25 by a dog showing distinct signs of hydrophobia. She was a large woman, and was bitten badly on right breast and over left external condyle. The dog unfortunately was killed. Patient's wounds cauterized. Complained of some pain and itching.

June 16, patient received 3 c.c. of virus at 11 A.M. and 3 c.c. at 6 P.M.; 6 c.c. given on June 17 and 18, then 2.5 c.c. up to July 4, and last dose given July 5. On June 21 the patient complained of pain in the left arm. The patient continued in good health.

CASE III.—This woman's daughter, aged five years, had been bitten by the same dog on the face near the eye. The child died in convulsions four weeks after receiving the injury, June 14, 1910; no virus had been administered.

CASE IV.—(Exposed.)   L. K., aged ten years. Admitted August 17, 1910. Was bitten August 12 on left leg below the knee; scar about three inches long, with the imprint of three teeth. A few drops of blood were said to have escaped from the wound. Dog positive for Negri bodies. The wound was cauterized and virus given as follows: July 18 to 21 inclusive, 2.5 c.c., two injections; August 21 to September 6, inclusive, one injection. These were given subcutaneously in the region of the abdomen. There was considerable inflammatory reaction from the injections. No signs of rabies developed.

CASE V.—(Exposed.)   A. F., Italian, aged fourteen years. Admitted August 31, 1910, to surgical department. Was bitten by a dog about 8 P.M. (in an empty house) on the left leg; there resulted a wound in this region about one inch by one-fourth inch, and a smaller one on the right forearm; also wounds on penis and bad ones on scrotum and right side of forehead.

The dog was not found, but on account of the description of its actions, and because of the nature and location of the wounds, the boy was admitted for treatment. The boy was brought to the hospital from another institution about 9 P.M. The wounds were cauterized and dressed. Twelve stitches had been inserted. Patient was given Pasteur virus subcutaneously on the abdomen as follows: September 6 to 9 inclusive, 6 c.c. (virus labelled day before), two injections from each bottle; September 10 to 29, 2.5 c.c. Discharged October 1.

CASE VI.—C. McC., male, aged twenty-seven years. Admitted April 13, 1910. Bitten one month previously on left hand. Was brought from another hospital. Would not eat, restless, had sore throat, bloody sputum. Pupils dilated and did not react to light; left pupil larger. Went into clonic convulsions for twenty to forty seconds every three minutes, started by trying to drink water and when the air struck him. Albumin positive. The patient was originally admitted to the alcoholic ward; thought outside the hospital to have delirium tremens. Died April 14, 1910. Treatment consisted in giving chloral and bromide by enema, morphine, and hyoscine hydrobromide. Postmortem examination of the patient showed merely congestion of the organs as might be expected in a case of rabies and Negri bodies.

CASE VII.—Similar to foregoing, but recognized before admission.

CASE VIII.—(Exposed.) M. H., female, white, mill hand, aged twenty-two years. Bitten just below right ankle. Dog positive for Negri bodies November 6, 1909. Virus given same as Case I. Patient well after three months without developing rabies.

CASE IX.—Sent to the hospital as a case of mania from another institution. Died in typical convulsions. History of bite from a pet dog elicited. Smears from patient's brain positive for Negri bodies.

We must be ever on the alert to weigh the reports of friends of the patient and look for exaggerations and untrained observations.

The last two cases were the only cases of pseudohydrophobia in our list. The point to be emphasized is the proper selection of cases really exposed to the poison and the institution at once of what we now know to be the best remedial procedures.

Since writing, other interesting cases have come to our attention, and have been accordingly studied, but not yet published.

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DISCUSSION

Dr. D. J. McCarthy: An important point in diagnosis is the period of incubation, which is usually about six weeks. In almost all the spurious cases of rabies I have seen the incubation period was much too early or very much too late. My feeling in examining a case of suspected rabies is that there should be worked out very carefully the question of exposure, the history of dog bite and an estimation made of the period of incubation. Should this period be four to seven weeks the presumption is that the case is one of real hydrophobia in contradistinction to one of those cases simulating the disease.

One condition mistaken for rabies and in which the similarity of symptomatology is very marked is that of enlarged thymus. In young children this is associated with rapidly destructive symptoms and closely resembles hydrophobia. I have seen autopsies in two cases. Both cases presented a clear symptomatology of rabies. In one case there was the history of dog bite seven months previous. There was difficulty in swallowing, irritability, slight rise of temperature, and the usual mental state. This persisted for several days, terminating in convulsions and death. In this case the thymus was very much enlarged with a tail-like portion extending up the thyroid. Inoculations were negative. It is interesting to work out the disease of the thymus later in life. In adults the hypertrophy of the thymus leads to a condition of myasthenia gravis.

I do not feel that it is necessary for Dr. Frescoln or anyone at the present day, in the light of our scientific knowledge, to defend the position that hydrophobia is a clinical entity. There are not only pathological lesions but also experimental evidence of the existence of the disease.

A possible error may be made in searching for Negri bodies in cases where hemorrhages exist near the ganglion cells. Eosin was used in the technique, and the absorption of the iron pigment may have accounted for the appearance of the condition simulating the Negri bodies. This ought to be borne in mind when only one or two specimens are studied.

Dr. Hobart A. Hare: For those Fellows of the College who may be interested in this subject I should like to call attention to an epidemic of rabies which occurred in the royal herd of deer near London in 1888. A number were at the Brown Institution, where I saw them with Sir Victor Horsley and Dr. Beaver. There was nothing extraordinary in the outbreak except that a rabid dog had inoculated a large number of the deer. The viciousness of the animals, which ordinarily are so gentle, was very marked. If this epidemic was reported the report must have been buried in some obscure publication, because in the United States Public Health and Marine Hospital records no mention is made of it.

When I wrote to the author he told me that he had not heard of this epidemic. These instances are of interest, I think, to anyone wishing to investigate the subject of rabies.

DR. WILLIAM S. WADSWORTH: The horror produced in the minds of those who come in contact with cases of this disease is enough to stir us to do our utmost to eradicate the disease. Every effort to attain a true knowledge of the disease and to spread a realization of its nature and the preventive measures required should receive the support of the profession. This should include not simply the treatment after symptoms develop, for such will be of little value, but should include the protection of the community from rabies in dogs and other animals and greater attention to the treatment of their bites.

I have come in contact officially with a number of cases and have investigated some suspected cases. The first case referred to me was clearly not hydrophobia, but most of the cases referred to us by physicians as hydrophobia have proved to be true cases. Several cases have turned out to be such that had been referred under different diagnoses. One group of cases was most instructive. A large dog ran along Ridge Avenue and bit a number of persons. Two of these died of hydrophobia; five others did not develop the disease. The first group had been treated by the abominable drug-store methods of so-called disinfection. The second group had been treated at one of our hospitals with strong carbolic acid.

I worked very hard over this series of cases and I am convinced that the failure to properly treat the wounds in the two cases that died was almost criminal. Also, I am convinced that the failure of the five cases to develop the disease was at least in some degree due to the cauterization with carbolic acid. I have not seen a case where the bite was quickly and thoroughly treated with strong carbolic acid. Of course, there remains much to be done before we can be sure about this matter, but it is of great importance, and the evidence is all in favor of strong carbolic acid.

The use of fuming nitric acid is probably good, but many would hesitate to pour it on a bite of the face of a child, and such hesitancy would be justifiable.

The use of trash that will not penetrate to the very bottom of the wound, that will not disinfect anything, and that does not go after the germ that is getting into the body should not be tolerated or further talked about. The larger field of prevention should have our attention, and we should be much more active in advocating all measures to prevent the spread of the disease.

European countries have already done remarkably well in preventive work. England had an alarming series of cases, but the central government took the matter in hand and instituted very rigid laws which almost

instantly caused the curve of frequency to drop and the disease was almost obliterated. Every community must have muzzling laws and stringent rules about animals running loose.

Fortunately Philadelphia has active dog collecting agencies that keep our streets remarkably free from stray dogs, but even there we can be of use in urging greater rather than less strongly observed rules.

We have no excuse for neglecting any of the means for eradicating this most terrible disease.

A few points about the disease may be of interest to the general practitioner. Many persons already possess an immunity such as would be produced by the Pasteur treatment. Dog catchers generally escape, though bitten often and by all sorts of dogs, and it is not unlikely that they acquire immunity from their bites. When the disease is developing it usually develops as the distance from the medulla to the bite. A face bite develops earlier than one on the hand or foot, so that there is less time to spare in cases of near bites to institute treatment. It is common for the bites to become sensitive before the disease becomes pronounced. The best treatment we know has been described by Dr. Frescoln.

I think we should, at this time, acknowledge our indebtedness to Dr. Leonard Pearson, who fostered the beginnings of the great work now going on here and to his followers, Dr. Ravenel and Dr. McCarthy, and those now carrying on the work of the State live stock laboratory, and also to those at the Philadelphia General Hospital. This work has put our city well to the front in science and practice in this field.

Dr. Astley P. C. Ashhurst said he wished Dr. Frescoln would tell the College what method of cauterization he had employed in the cases reported tonight. It was worthy of notice, he thought, that of these cases only those patients recovered whose wounds had been properly treated; and that patients whose wounds had not received proper treatment had died in spite of the use of the Pasteur treatment. Dr. Rambaud, head of the Pasteur Institute in New York, claimed that cauterization was useless unless the actual cautery was employed, and considered bichloride of mercury (1 to 1000) the best antiseptic. It has been suggested that lemon juice might be employed in an emergency, as this has been found of value in experimental work. If it were certain that the bite had been inflicted by an animal which was really rabid, a cupping glass should be applied to the wound, or this should be sucked, so as to extract the virus; and its absorption might be delayed by the use of an elastic tourniquet. All such measures, the speaker said, seemed to him to be of more prophylactic value than the Pasteur treatment.

DR. FRESCOLN: In answer to the inquiry I would say that fuming nitric acid was used immediately to cauterize, or in other cases, crude carbolic. There are on the table photomicrographs of the Negri bodies.

COMPENSATION BY DISPLACEMENT OF THE THORACIC VISCERA IN PULMONARY TUBERCULOSIS.[1]

By CHARLES LESTER LEONARD, A.M., M.D.

THE laws of physics render it essential that the lungs shall follow the thoracic walls and the diaphragm in their movements. This is because the lungs are distensible, flaccid organs, open to the inrush of air, placed within a closed and semirigid bony and muscular case, which is capable of increase and decrease in its volume by muscular movements. Any alteration in the capacity of the lungs must be compensated for, or the excursion of the walls surrounding them must be decreased.

Compensation for the loss of expansion in the lungs takes place through an increase in the capacity of their normal area, or through the interposition between the visceral and parietal pleura of an area filled with air or fluid, or both. These changes must take place in proportion to the volume of the lungs involved in a pathological process. They are, in a measure, appreciable by the ordinary methods of physical diagnosis. The changes which can be noted by inspection and mensuration are, however, less marked in ratio with the extent of the disease in its early stages than those within the thorax, which produce displacements or alterations in the position of the viscera.

Tuberculous disease must be far advanced, or an acute pneumo-, hydro-, or pyothorax of large volume must be present before the limitation of the thoracic movements can be noted by inspection.

Marked alterations in the position of the interthoracic viscera occur in the earlier stages of tuberculous disease, without visibly changing the excursion of the thoracic walls. These displacements occurring early in the disease have been generally overlooked. Until recently it was held that the heart and greater bloodvessels were so firmly attached by ligaments to the skeleton and diaphragm that they could not be displaced except under extreme conditions. These views were apparently upheld by the postmortem findings.

Since they have been recognized by the Röntgenologist in the living subject, it has become evident that the postmortem changes hid the true condition. The correctness of this conclusion was shown as the result of a discussion, which I had in 1909, with an internist connected with one of the largest institutions for the special study of tuberculosis. He did not believe that displacements of the viscera could occur so frequently in the earlier stages of the disease. He said that in some hundreds of postmortems conducted at the institute they had failed to find such displacements. Some months later he told me that in the subsequent 100 postmortems they had found 25 or 30 displacements in the less advanced cases.

These pathological variations in the position of the thoracic viscera can be clearly shown only by the rapid Röntgenogram that eliminates the heart's motion. Their exact position and interthoracic relations can only be fully appreciated by the rapid stereoröntgenogram.

The 12 cases used in illustrating the subject of this paper are taken from a series of 100 cases studied by the rapid röntgenogram. These cases were, for the most part, referred for examination from the State Dispensary for Tuberculosis, through the kindness of Dr. A. P. Francine, and a part of them formed the basis of a paper read by me before the British Medical Association in 1908.[1]

Many, however, including some of the more interesting pathological cases, were from private practice.

[1] British Medical Journal, September 12, 1908.

In the entire series of 100 cases 26 displacements of the heart and aorta were found, with 3 cases of pneumothorax. In 17 cases the heart was displaced to the right; in 4 to the left; and in 5 a rotation took place with an upward displacement of the heart and aorta, so that the heart assumed an anteroposterior position. In 2 cases a superficial pneumothorax was found overlying the lower left lung, and in one case an acute hydropneumothorax of tuberculous origin was shown.

It is practically impossible to reproduce the Röntgenogram in ordinary printing with sufficient clearness to make its interpretation valuable. The 12 cases cited as illustrations of the subject of this paper have, therefore, been reproduced in tracings made directly from the individual Röntgen negatives. Varying types of line drawing have been used to diagrammatically represent the different stages of the pathological process.

An increased number of lines in one direction represent the line of contractile force. The tracings are accurate in detail, and can be more readily appreciated by the reader. The accompanying stereoröntgenograms, if viewed through the ordinary parlor stereoscope, will show in a measure the wealth of detail which can only be fully appreciated by the study of the original negatives on the large stereoscope.

The sharp outline of the heart, seen in these plates, shows that the exposure must have been sufficiently rapid to eliminate its motion; that is, they must have been taken in a fraction of a heart's beat. The time between the stereoscopic pairs, required to shift the plates and tube, was one-half second. The total time for both exposures was, therefore, less than one second.

A review of the cases in the entire series shows that those cases in which no displacement of the viscera was present were early lesions, in which no fibroid change had taken place, or that the lesions were not extensive and symmetrical, or that the heart was bound down by adhesions between the pericardium and the diaphragm.

The unequal elevation of the two halves of the diaphragm, Williams' sign, was present in less than one-half of all the cases,

and was not present where displacements of the interthoracic
viscera had occurred.

The irregularities of the diaphragm seen in the cases illustrating
this paper are due to adhesions between the pulmonary and
diaphragmatic pleura.

The pathological displacements of the thoracic viscera in
pulmonary tuberculosis are the result of compensation for the
destruction of expansile normal lung tissue by the disease.

The displacing force is the result of one or two changes or the
combination of both, or as in the case of acute hydropneumo-
thorax from the rupture of the lung. The consolidated lung area
may undergo fibroid change and contraction, the contracting
tissues drawing the heart and aorta with them, while the emphy-
sematous lung on the opposite side assists in their displacement.
That these two causes can act separately or together is shown in
the illustrating cases. In some the heart and aorta are displaced
in a direction entirely different from that of the pressure exerted
by the emphysematous lungs or even when a marked emphysema
is absent. Again, a displacement is present and an extensive
emphysema alone accounts for it.

In the surgical treatment of ordinary abscesses, evacuation and
drainage are followed by compression by the external dressing,
to bring about coaptation of its walls and healing. Since external
pressure cannot be exerted within the thorax, the same result is
achieved in the natural healing of abscess cavities in the lungs by
the displacement of the viscera to produce compression.

In addition to the displacements which cause compression of
the diseased portion of the lung, there is present in many cases an
ossification of the costal cartilages and an approximation of the
ribs over the affected area. As I have suggested in a previous
paper, the ossification of the cartilages may be a process of anky-
losis to limit the motion of the ribs and place the parts more
nearly at rest.

The compensating displacements may be divided into four
groups. Displacements of the lung by superficial pneumo-
thoraces; displacements of the heart upward and into an antero-

posterior position; displacements of the heart and aorta to the
left; and displacements of the heart or heart and aorta to the right.

DISPLACEMENTS DUE TO PNEUMOTHORACES.   In both the cases
of superficial pneumothorax the physical examinations which
preceded the Röntgen examination failed to detect them, but
their presence was confirmed by subsequent physical examinations.
In both cases the primary lesion was of the left upper lobe, with
no involvement of the right lung.   It is noteworthy that in none
of the similar lesions of the entire series which involved the upper
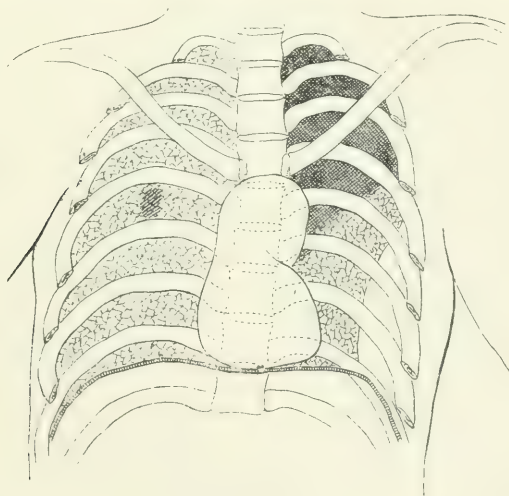
FIG. 1.—Case I.

right lobe did a pneumothorax occur.   The accompanying stereo-
röntgenogram of Case I shows the lower lobe of the left lung
hanging like a lace curtain within the thorax, conforming to the
curve of the thoracic wall and separated from it by an area clearly
devoid of all lung structure.   The upper left lobe shows distinct
lines of fibrosis in the infiltration, while peribronchial lymph nodes
are seen in both lungs.

A later stage of a similar lesion is shown in Case II, but with
an entire absence of peribronchial enlarged glands.   In this case
the entire left lung is involved.   The cavity seen in the upper

lobe shows that the older lesion was there. The lower lobe is
compressed, but not entirely consolidated, and is covered with
a distinctly thickened pleura, which can be seen in the Röntgeno-
gram. In marked contrast to the succeeding case of acute hydro-
pneumothorax, the heart and aorta are displaced to the left,
probably entirely as the result of the compensating emphysema
of the entire right lung.
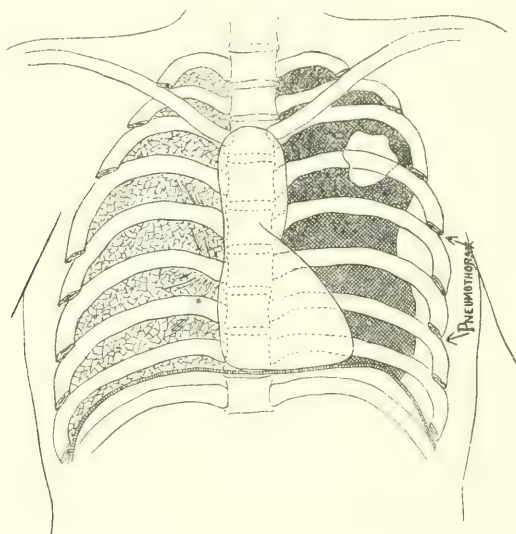
Fig. 2.—Case II.

The next case (III) was of particular interest, as it was an acute
tuberculous hydropneumothorax. This Röntgenogram was taken
with the patient in the erect position, because of the fluid, which
is seen as a level line just below the seventh rib. The lung is
compressed upon the mediastinum and the heart and aorta are
displaced to the right. This condition was readily recognized
by the physical examination, but the position of the heart and
aorta were not definitely determined. In this case both the
lung and the heart with the aorta are displaced to the right.

ANTEROPOSTERIOR AND UPWARD DISPLACEMENTS. This dis-
placement was found in 5 cases of the entire series, as illustrated

in this paper by Tracings 4 and 5. The tuberculous lesions in all
these cases were symmetrical and involved both upper lobes. The
heart was not only rotated, but with the aorta was drawn upward,
showing that a decided force was exerted by the contracting
fibrous tissue in the upper lobes. It is possible that the decreased
superficial area of the heart presented to percussion in these cases
may account for an old opinion that the heart is small in tuber-
culous subjects. This opinion was not confirmed by the compari-
son between the size of the heart and the body weight of the
patients in the entire series.
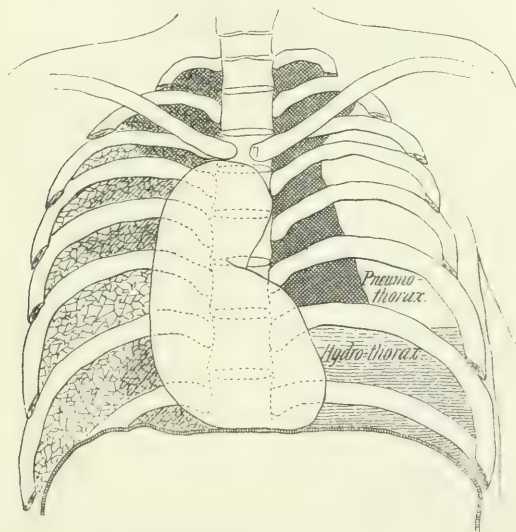
FIG. 3.—Case III.

In Case IV the heart is drawn up and rotated, so that as it
rests upon its apex it presents a peculiar aspect as a wide band
occupying the mediastinum.

In Case V the rotation is not so complete and the band of
mediastinal shadow is broader. In the stereoröntgenogram of
this case it will be seen that the heart lies within a very much
thickened pericardium, upon the left side particularly, which
accounts for the peculiar straight line shown as its left border.

The heart, however, can be distinctly seen within the pericardial shadow. The stereoscopic picture also shows very clearly a dilated bronchus forming a cavity in the right upper lobe, with the surrounding infiltration and fibroid change in both upper lobes, with commencing softening and cavity formation in the left upper lobe.
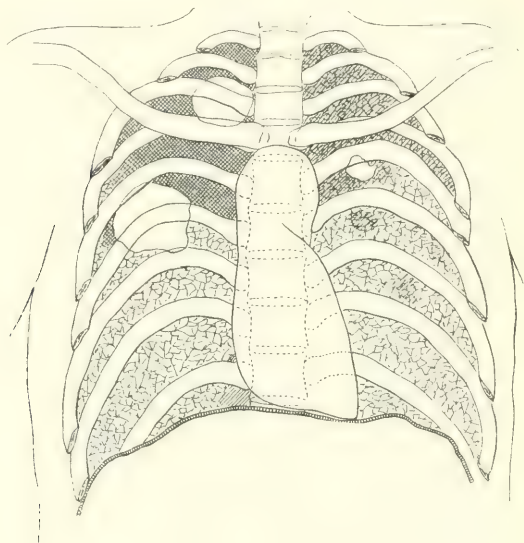
FIG. 4.—Case IV.

In the entire series of cases the displacement of the heart to the right was four times as frequent as the left in direct opposition to the opinion expressed by some authors. Of the greatest importance to the clinician is the fact, first demonstrated by the Röntgenologist, that the aorta is also displaced in almost every instance. It is possible in most cases to demonstrate by percussion the border of the displaced aorta that lies outside the line of the sternum, but almost impossible to show the one that lies beneath it. This fact has undoubtedly led to the diagnosis of aneurysm in many cases of displaced aorta. In only one case of the entire series was an aneurysm found. It was suspected from the symp-

toms presented, but could not be demonstrated by physical examination. The Röntgenogram showed an aneurysm buried in a mass of tuberculous consolidation that occupied both upper lobes and a part of the lobes below them. In contrast to this is Case VIII, to be spoken of later, in which the symptoms suggesting aneurysm were found to be due to a displaced aorta.
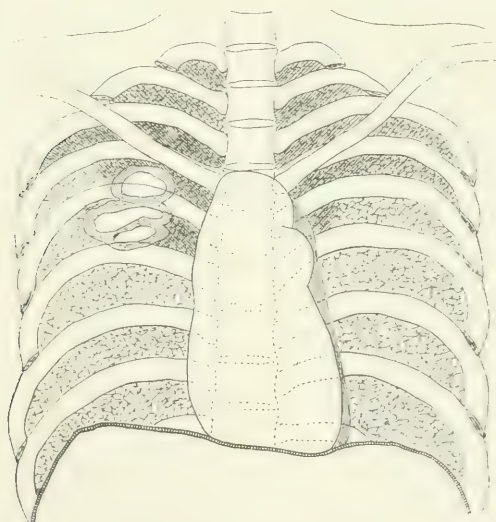
Fig. 5.—Case V.

DISPLACEMENTS OF THE HEART AND AORTA TO THE LEFT. In addition to Case II, of superficial pneumothorax, where the heart and aorta are displaced to the left, this group of displacements is illustrated by Case VI. Here there is an extensive involvement of the left lung. There is a cavity with surrounding consolidation and softening in the upper lobe, while consolidation and marked fibrosis have taken place in the upper portion of the lower lobe. The heart is drawn well over to the left, but the arch of the aorta is in its normal position.

DISPLACEMENTS OF THE HEART AND AORTA TO THE RIGHT. The extent to which the heart and aorta can be displaced upward and
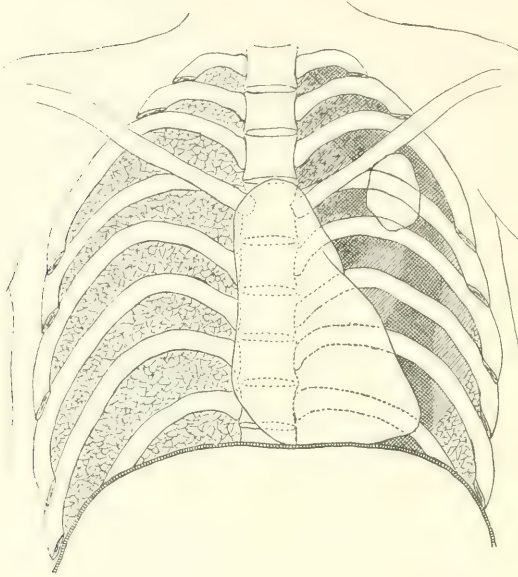
FIG. 6.—Case VI.
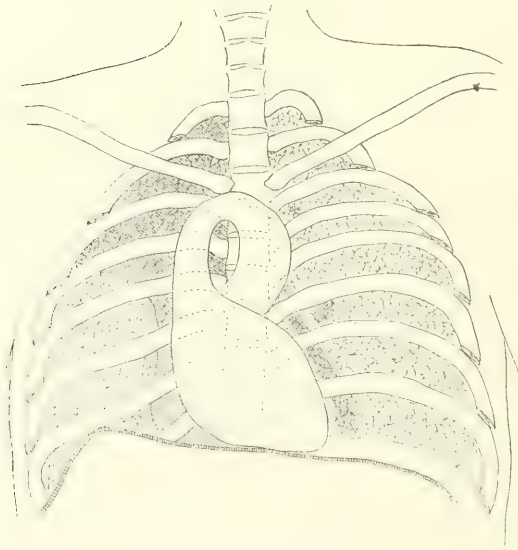
FIG. 7.—Case VII.

to the right, by fibrosis and contraction of a diseased area limited
to the right upper lobe, is clearly illustrated in the stereoröntgeno-
gram of Case VII. The heart and ascending aorta are drawn up
so far that the arc of the arch is increased and the separation from
the descending aorta is so great that one can see through the arch.
The right lower lobe is emphysematous, and presents upon its
lower surface a dome-like protrusion of the diaphragm, evidently
due to a localized adhesion of the pleura. The left lung shows no
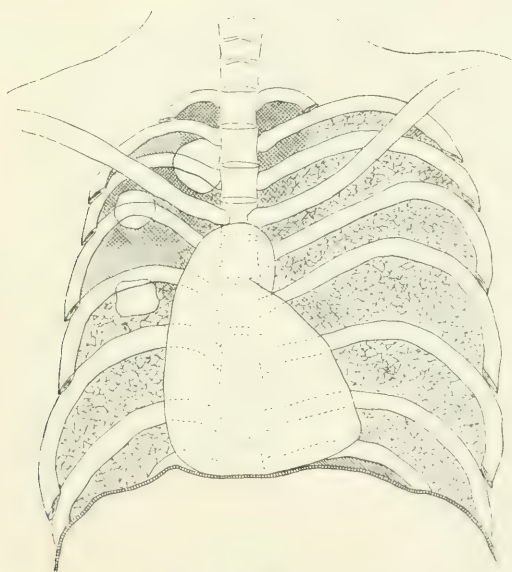
FIG. 8.—Case VIII.

compensatory emphysema, but lines of infiltration and foci of
tuberculous disease can be seen scattered through it, especially
on stereoscopic examination.

The displacement of the heart and aorta in Case VIII gave
rise to symptoms which led the laryngologist to suspect the pres-
ence of an aneurysm in an evidently tuberculous subject. In
addition to a paralysis of the vocal cord the case presented other
very interesting features, and has been reported in detail by

Dr. E. L. Van Zant, before the Laryngological Section of the
College, by whom it was referred for Röntgen examination. The
Röntgen plates showed that no aneurysm was present, but that
the heart and aorta had been displaced far to the right. The
tuberculous lesion was confined chiefly to the right upper and
middle lobes, where consolidation fibrosis and cavity formation
has taken place.

Thickened Pleura
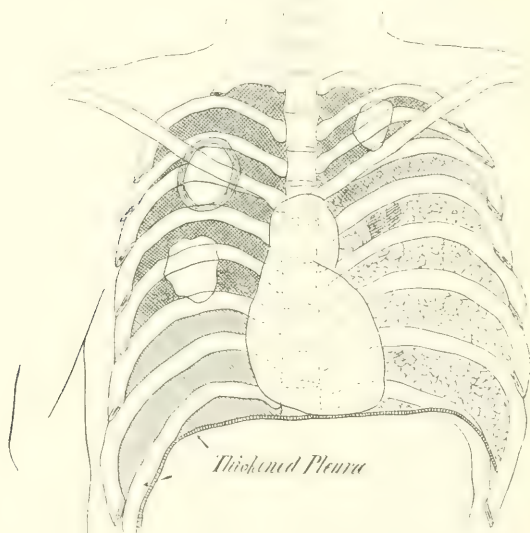
FIG. 9.—Case IX.

The multiple lesions of a rapid tuberculous process, as well as
a moderate displacement of the heart and aorta to the right,
are shown in Case IX. Here we have infiltration, consolidation,
fibrosis, an old walled cavity, the breaking down of tissue to form
a cavity, a cavity in the left upper lobe without a thickened wall,
and an area of the lower right lobe covered by thickened pleura.

The remaining cases are illustrations of displacements to the
right of the heart or heart and aorta, and are the type of cases
readily recognized and termed dextracardia. Displacement of
the aorta to the right is also present, but had not been deter-

mined by the physical examination, while Case XII is the only case in the entire series in which displacement of the aorta did not occur with the displacement of the heart.

The moderate displacement of the heart and aorta to the right in Case X can be accounted for by the adhesion of the pericardium to the diaphragm and the general fibrosis which has accompanied the miliary tuberculosis.
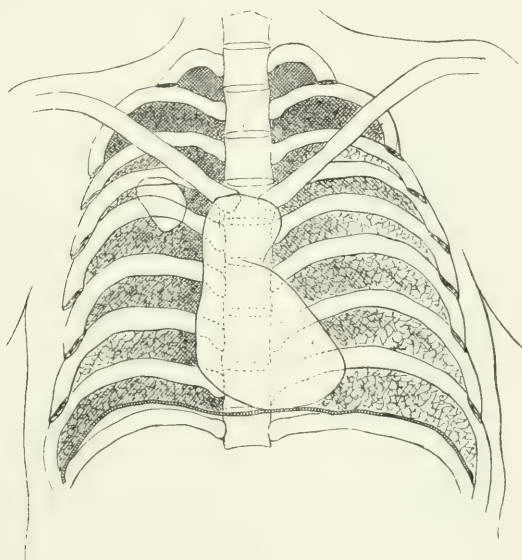
Fig. 10.—Case X.

The small masses of miliary tubercle are seen distinctly, especially in the original negative and the lantern slide, scattered throughout both lungs, accompanied by bands of infiltration. The upper right lobe is consolidated, with fibroid change and cavity formation.

The wide displacement due to consolidation of the entire right lung with fibroid contraction and emphysema of the left lung is illustrated by Case XI. The original seat of the disease is shown by the advanced fibroid change in the right apex and the cavity formation. The heart and aorta are drawn far over to the right

and slightly upward. The spread of the disease to the left lung is seen in infiltration and early cavity formation in the left upper lobe.

Another illustration of dextracardia with advanced fibroid change is shown in Case XII. The apex of the heart is displaced nearly to the median line. In this case, however, we find the arch of the aorta in its normal position. This absence of displacement is probably due to the general fibrosis which is evident throughout both lungs and the absence of consolidation and extensive fibrosis
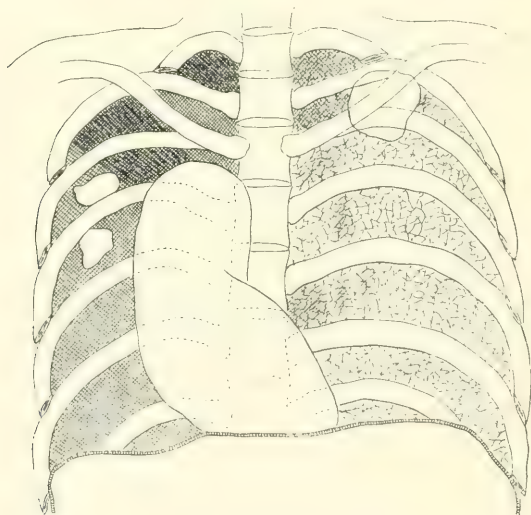
FIG. 11.—Case XI.

of the right upper lobe. This is the only case where the aorta was not displaced, and also the only one of displacement to the right in which the right upper lobe was not extensively involved by the disease.

In all the cases illustrating this paper, and in the entire series from which they are taken, the clinical findings have been compared with the Röntgen diagnosis, and the points brought out alone by the Röntgen examination have been subsequently confirmed by a physical examination.

The Röntgen method of examination has been shown to add to the knowledge obtained by other methods of physical diagnosis, by detecting superficial area of pneumothorax, by showing that the aorta is generally displaced with the heart, and by making evident the effect of fibroid change in displacing the viscera through its contraction. In addition it is a valuable mechanical method of observing and recording the changes, and displacements produced within the thorax by tuberculous lesions of the lungs. It also assists in the understanding of the processes of repair which
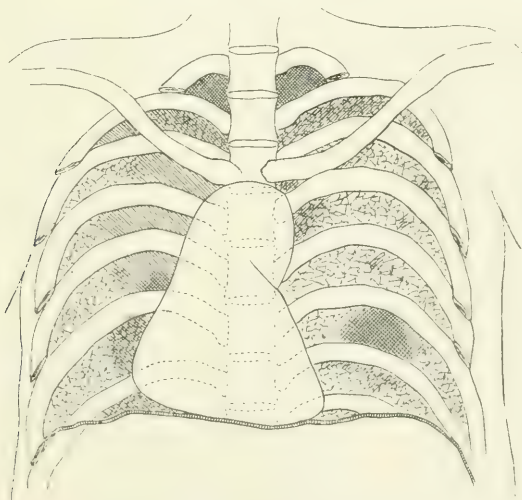
Fig. 12.—Case XII.

take place in the closing and healing of old cavities, while it forms a permanent record for comparison with that obtained in later examinations, thus showing the progress of the disease or of the process of repair.

It is self-evident that Röntgenoscopic examinations of the thorax and lungs, that is, the visual examination by means of the Röntgen rays and the fluoroscope, cannot afford accurate permanent data such as are secured by the rapid Röntgenogram, and particularly the stereoscopic Röntgenogram. There can be no

doubt that viewing with the fluoroscope is a cheaper method and
that it is less accurate, since it gives data that are only visible to
the eye of one observer. It possibly affords an advantage in view-
ing the movements of the diaphragm, but it cannot eliminate the
effect of motion produced by the heart's beat, and does not show
the minute detail essential to a careful diagnosis. An examina-
tion sufficiently long to enable the observer to gain any valuable
information must necessarily expose the patient to the rays for a
far greater period than the second or two required for the rapid
stereoröntgenogram.

The series of cases illustrating this paper in tracings, stereo-
röntgenograms, and lantern slides show the contribution which
röntgenology has made to the knowledge of the pathological
displacements of the thoracic viscera produced by the lesions of
pulmonary tuberculosis.

DISCUSSION.

DR. HENRY R. M. LANDIS: I should like to ask Dr. Leonard how
many cases came to the autopsy table, because even when the clinical
results and the x-ray plates have been compared, experience has shown
that a different condition is sometimes present. I should also like to
ask whether the pneumothoraces were recognized by clinical examination
or by the plates only. I should think it would be difficult to detect any
displacement of the aorta by clinical means, and I should like to inquire
how often the clinical examination of displacement of the aorta coincided
with that found in the x-ray examination.

DR. JAMES M. ANDERS: I was somewhat surprised to hear the state-
ment made in the paper that the heart is displaced toward the right
four times as frequently as toward the left in pulmonary tuberculosis.
In making physical examinations in cases of tuberculosis, one is led to
believe that the heart is displaced toward the left, because the left lung
when retracted uncovers an increased area of the anterior surface of the
heart, giving the impression that the latter is displaced toward the left.
At all events student clinicians oftentimes make the diagnosis of displace-
ment of the heart toward the left and quite as often of hypertrophy of
the heart when in reality it is simply uncovered as the result of disease
of the left lung. This group of cases is readily eliminated by the x-rays.

Dr. Leonard has pointed out that in the vast majority of cases in which there is displacement of the heart toward the right, the aorta is also displaced; this had not been discovered by the clinician prior to the introduction of the x-ray method of studying cardiovascular diseases. It is always extremely difficult, and perhaps in most cases impossible, even when the x-ray examination shows the condition of right-sided displacement of the aorta, to recognize it by means of the physical signs. I think we have here an instance in which the x-ray examination is a positive advance over the older methods of physical examination. One reason why the heart is displaced more frequently toward the right than toward the left is doubtless because of the fact that the hydropneumothoraces are more common on the left than on the right.

DR. LEONARD: In answer to the inquiry, the superficial hydropneumothoraces were discovered by the physical signs only after the x-ray examination showed them to be present.

The displacement of the aorta and of the heart to the right in this particular series of cases has been more frequent than to the left, and the fact that we have the peculiar position—the anteroposterior position produced by the heart—has led me to believe that in many cases the supposed frequent occurrence of a decrease in the size of the heart in tuberculous cases is rather due to a change in the position of the heart than to a change in the size. As Dr. Anders has said, the drawing away of a portion of the lung from the right has led to the idea of its hypertrophy.

I have not studied these cases from the internists' point of view, that was done by the internists, but rather from the x-ray standpoint. We have compared all the cases with the clinical findings, and the result of the x-ray finding is what I have presented in this paper.

CECUM MOBILE.[1]

By JOSEPH SAILER, M.D.

By cecum mobile is meant an abnormal motility of the cecum and lower portion of the ascending colon. This may be purely anatomical and give rise to no clinical symptoms, or, as a result of movement of the cecum, kinks may be produced causing partial or temporary obstruction that ultimately gives rise to more or less atony and dilatation of the cecum with associated clinical symptoms.

The term was first employed by Haussmann, who, in 1904, reported 8 cases characterized by fairly similar clinical signs the cause of which he ascribed to this abnormal condition whose existence he determined purely by physical examination.

The various malpositions of the large bowel have been the subject of attention on the part of anatomists for many centuries, and Schultz has collected the description of these anomalies in Morgagni's writings.[2] Curschmann, in 1894, was the first to attempt a systematic study of the possible relation of these malpositions to various clinical manifestations. In the course of this article he describes several cases of reflection upward of the cecum with a sharp kink that caused complete obstruction; in one instance the blind end of the cecum was close to the edge of the liver. He was able to demonstrate that anomalies of the

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[1] Read November 1, 1911.

[2] Case 14. "The beginning of the ascending colon lay deeper than normal." Case 19. "The ascending colon was so bent and doubled upon itself that the fundus of the cecum, directed upward, touched the portion of the transverse colon lying under the liver." Case 3. "The colon overlying the small intestines passed upward from the right hyperchondrium to the umbilicus." Vesalius has pictured the reflection upward of the colon.

mesentery and mesocolon were responsible for these displace-
ments, and therefore indirectly for the clinical symptoms. He
noted also that when the attachment of the mesocolon of the
cecum to posterior parietal peritoneum did not occur, the cecum
might be found in the region of the umbilicus, giving rise to a
"Wander cecum" or floating cecum.

Haussmann's 8 cases were all characterized by attacks of
colic, usually beginning with constipation, and the presence during
the attacks of a movable tumor in the right lower quadrant of
the abdomen that could be pushed upward leaving an empty
space in the right iliac fossa. The number of his cases has since
been increased to 143, none of which, curiously enough, at the
time of his last publication, had been confirmed either by autopsy
or operation, chiefly, he complains, because consultants did not
recognize the existence of the condition, and therefore would
not concur in the diagnosis. His paper attracted very little
attention, and it was not until Wilms reported 40 operative cases
that the physicians of Germany began to regard cecum mobile
as an actual clinical disease. He had observed that many cases
of so-called chronic appendicitis were not relieved by appendec-
tomy, particularly if the appendix was not adherent, and inferred
that his inability to obtain statistics regarding the end results
of operations for chronic appendicitis was due to the uncertainty
and indefinite character of the benefit derived from them. It
occurred to him, therefore, that other factors than disease of the
appendix might be active in causing the symptoms, and after
some study he reached the conclusion that the pain at least might
be due to a long cecum mobile. This might permit the stretching
or tearing of the nerves in the mesentery and mesenteriolum,
and at any rate be responsible for the tenderness at McBurney's
point. Those cases in which the appendix and cecum are freely
movable are theoretically not curable by appendectomy alone,
and accordingly he devised an operation for the fixation of the
cecum by means of broad adhesions to a sort of pocket formed
in the iliac fossa. In 40 cases this gave good results.

The observation of Wilms that operations in cases of so-called

chronic appendicitis failed in many cases to relieve the symptoms had been frequently made by clinicians prior to the publication of his article. Albu, in particular, had called attention to this point, although he did not suggest any satisfactory explanation. It is noteworthy that in the text-books of neither Deaver nor Kelly are any statistical studies made of their operative work in these conditions, although the experience of both must be very large.

In the brief period that has elapsed since Wilms' article, cecum mobile has excited the liveliest interest among the German and Russian internists and surgeons. Fischler, in 1909, was able to report 41 cases and to give the first comprehensive description of the symptoms from the medical standpoint, and Klose, in a series of articles published in 1910, again discussed the diagnosis and reported the results of surgical measures in 12 cases. Of these 12 the first 7 were discovered only after the abdomen had been opened, but with the experience gained from these the last 5 were diagnosticated before operation. Neimann, Heiler, and Straschenko have also reported cases and discussed the condition. So far as I know, it has not attracted the attention of French, English, or American medical writers.

The anatomical basis appears to be a congenital malformation of the mesocolon of the cecum, of such a nature that for some distance along the ascending colon it maintains the type of the mesentery and is not attached to the parietal peritoneum.[1] This permits to the part at large all the freedom of movement characteristic of a loop of small intestines, and, indeed, as a result of the greater length of the mesentery and the less confined position of the first portion of the colon, considerably greater displacement may take place. That this malformation occurs, as the Germans contend, in the latter part of the second month of pregnancy appears to me to be an illogical assumption. It first becomes manifest when the primitive gut begins to differentiate, but the predisposition must exist from the beginning of independent

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[1] This condition usually extends for from one-half to two-thirds of the length of the ascending colon according to Wandel, and in six of his seven cases as far as the liver.

embryonal existence. This defect of the mesocolon is, of course, not in itself a morbid condition, and may exist without giving rise to any clinical manifestations whatever, but it renders certain forms of obstruction possible that cause the attacks and secondarily the distention and atony of the cecum. These obstructions are of three types: (1) The formation of a kink usually near and below the hepatic flexure; (2) the reflection upward and forward of the cecum upon the ascending colon until, indeed, in the most extreme cases, the caput coli may touch the liver; (3) volvulus of the cecum. Two cases of the second type and one of the third type were reported by Curschmann. These, however, are not the only lesions that may give rise to these symptoms for not less than 3 of Klose's 12 cases showed at operation adhesions pulling the cecum downward and thus producing obstruction.

Haussmann recognizes two varieties: (1) passive mobility, and (2) spontaneous mobility. The latter is subdivided into three types according to the level to which the caput coli can be displaced—to the crest of the ilium, above the crest, and to the costal margin. I have yet to observe a case in which I could demonstrate to my satisfaction any such extreme motility as in the third type.

There appears to be much difference of opinion regarding its frequency, a difference due in large part to varying standards. It is, therefore, impossible to compare or even to attempt to reconcile the figures that have been given by various investigators. Thus, an abnormally movable cecum was found by Engel in 10 per cent. of the subjects he examined; Treves found extreme motility in 11 of his 100 dissections; Dreicka found a common mesentery of the ileum and cecum in 23 per cent. of the cadavers that he examined. The most important statistics are those given by Wandel. In 640 autopsies carefully studied with reference to this particular point, he found in 66 mobility of sufficient degree to permit kinking, torsion or displacement; of these, 28 were children, and although the whole number of children examined is not given, it is stated that the proportion is

greater than in adults. In 8 of the 66 cases, the cecum was turned forward and upward, but in the majority the position of the organs was normal. In regard to the frequency with which symptoms are produced, I have found only one definite statement. During the period in which Klose and Rehn operated upon 12 cases of cecum mobile, they also operated upon 80 cases of chronic appendicitis; that is, 15 per cent. of all supposed cases of chronic appendicitis may be due to cecum mobile.

The figures of Haussmann—143 cases observed in six years— indicate an enormous clinical material, a readiness to make the diagnosis, or a singular blindness on the part of the whole medical profession to a very common condition. Fischler gives no definite figures, but is content to surmise that "a large part of the troubles heretofore collected under the name of chronic appendicitis is due to a more or less pronounced muscular insufficiency of the cecum, a typhlatonia." He has observed 41 cases, but fails to state in how long a period, or what proportion they formed of his other cases. Indirect evidence may be found in the article of Wandel who has collected from the literature a large number of cases of volvulus of the cecum and ascending colon which were only possible as a result of their abnormal mobility.

There appears to be some difference of opinion regarding the symptomatology of these cases. According to Fischler the clinical picture is fairly uniform. Attacks of colic occur at irregular intervals, but with a general tendency to increase in frequency, severity, and duration. Each usually begins with a longer or shorter period of constipation and there is severe pain lasting for a few hours, about two according to Klose, or more rarely for several days, and terminating in a copious discharge of feces. During the attack there is loss of appetite and perhaps nausea and even vomiting; the temperature is either normal or, if fever occurs, it is slight. The leukocyte count is normal. A mass can be felt in the right lower quadrant about the size of a small apple, firm, but not hard, and elastic, but not doughy. Nothing can be felt on the left side. Tenderness is usually present and is most distinct near McBurney's point. Gurgling can usually be elicited.

Posture has a pronounced effect upon the pain. If the patient stands or sits the pain is worse; it is relieved and indeed the attack may sometimes be terminated if the patient lies upon the back or particularly upon the right side. Predisposing factors are exertion and the indulgence in food that produces flatulence. During the interval the patient may be subjectively well, but usually symptoms of chronic colitis are present; that is, alternating diarrhea and constipation, mucus in the stools, and intestinal flatus. In spite of Fischler's large experience, it seems that such a characteristic clinical picture cannot be present in the majority of cases, and I am, therefore, more inclined to agree with Wiemann, who believes that obstinate constipation not yielding to laxatives is the most characteristic feature. Haussmann is more interested in the physical examination of his patients than in the symptomatology. Klose apparently considers that the symptom complex ascribed to chronic appendicitis is also the symptom complex of cecum mobile.

The physical signs are those by which the displacement, the distention, and the atony of the cecum are recognized. They may be divided into signs obtained by palpation, by inflation of the colon, and by the x-rays. That the cecum can be palpated in a large percentage of cases is no longer a matter of dispute. Clinicians have obtained somewhat different figures, depending upon their skill and material, since Franz Glenard first described the boudin cecale. Obrastow in 109 men found a palpable cecum 56 times, or in 51.4 per cent., and in 60 women, 35 times, or 58 per cent. Haussmann claims to have palpated the cecum in no less than 256 of 300 persons, or in 80 per cent.

In order to test this subject I have analyzed the results of the physical examination of the abdomen made upon 312 office patients within the last year. The conditions of the examinations in all these patients were approximately the same. They were all ambulant patients and represented a considerable variety of clinical conditions, many of them having no symptoms referable to the abdomen whatever. Sixty-two, or about 20 per cent., had a distinctly palpable cecum. This varied from a soft, indefinite,

movable mass to a distinctly palpable, tympanitic, balloon-like body. The position was variable, in some cases nearer the anterior superior spine, and in others nearer the median line. The lower edge, as determined by palpation and percussion, varied between a point 2 inches below the interspinal line to a point 1 inch above it. In many cases no note was made of its exact position, and therefore the frequency of these variations cannot be given. In 19 of these 62 cases, that is, in about 30 per cent., there was more or less tenderness. As a rule, this amounted merely to some discomfort upon deep firm pressure, and was not associated with flinching or rigidity. Tenderness of this character was not recorded as such unless it was not present simultaneously on the corresponding point on the left side. In a few cases there was slight rigidity. There were no cases of certain acute appendicitis seen in the office. In 52 cases, about 17 per cent., there was slight tenderness of about the same degree over McBurney's point, not associated with a palpable colon. This was frequently variable, being found only once in a series of observations. At other times it was more or less constant, and probably indicated the existence of a chronic appendicitis or of some other inflammatory lesion in this region.

In the atonic condition the cecum is felt as a somewhat indistinct cylindrical or pear-shaped mass that can be passively displaced. It is usually tender, but rigidity and flinching are rarely observed. If present they suggest an inflammatory complication. Gurgling on pressure is a characteristic sign; splashing is rare. It may be possible to cause air to pass through the ileocecal valve into the ileum according to Hertz's method, but this would be at best difficult to recognize. A diminished resistance just below McBurney's point or a hollowness of the iliac fossa due to the upward movement of the cecum has also been noted by Haussmann. Inflation gives rise to two signs—disproportionate distention of the cecum and more or less evidence of insufficiency of the ileocecal valve. Regarding the former the explanation of Anschütz appears to have been unreservedly accepted.. This is as follows: If two dilatable bodies

with walls of the same elasticity are subjected to the same dilating force, the degree of dilatation is proportionate to the squares of the diameters. That is, if the lumen of the cecum is two or three times as great as that of the transverse or descending colon, the former will be dilated from four to nine times as much. Evidence of insufficiency of the ileocecal valve is the tympanitic distention of the central parts of the abdomen. This condition was carefully studied by Hertz, who ascribed to it the symptoms of constipation and flatulence. He also observed, in 1902, cases that might now be diagnosticated as typhlatonia or cecum mobile. The experimental inflation of the colon in these cases nearly always precipitates a characteristic attack.

The information yielded by the x-ray pictures of the colon has been studied carefully only by Klose. Ordinarily at the end of twenty-four hours a suspension of bismuth taken by the mouth is found in the descending colon and the rectum. In cecum mobile it remains in the cecum for two or three days. This finding, however, is only significant if associated with other clinical manifestations of the condition, and, if absent, cecum mobile cannot always be excluded, for at the end of an attack the bismuth rapidly disappears from the cecum. I am inclined to believe that this will also be found to be true during the normal intervals. Straschenko believes that x-rays are of little aid in the diagnosis. I have had x-rays taken of 5 cases in which I suspected cecum mobile for the purpose of determining whether bismuth persisted in the cecum for more than forty-eight hours. Four cases were positive and 1 negative. In all the positive cases the persistence of the bismuth in other portions of the colon, especially the transverse and descending colon, was quite as marked as it was in the cecum, although, as can be seen from the illustrations, the cecum appears to be a region of particular accumulation, and there is a somewhat clearer area in the neighborhood of the hepatic flexure. This accumulation in the transverse and descending colon is not noted by Klose, perhaps because he considers it comparatively unimportant or because it did not occur. It is, in my experience, and in the experience of Dr. Pancoast and

Dr. Pfahler, not uncommon. It seems to me that it suggests that possibly more factors than the motility of the cecum and lower part of the ascending colon are involved in these cases.

The clinical picture is still, as Wiemann says, uncertain. The differential diagnosis is as yet based rather upon theoretical than upon practical considerations. Cecum mobile is commonly mistaken for chronic appendicitis, and the distinction is rendered more difficult by the probability that the appendicitis forms a frequent complication. As Klose and Rehn, and Wilms, the only surgeons to report any number of cases, invariably remove the appendix, its role in the production of the symptoms can only be guessed. Wilms, however, in 5 cases removed the appendix and did not fix the colon, and none of them were benefited by the partial operation. For the direct diagnosis Wilms depends upon the possibility of bringing the cecum to a position in front of the wound. Klose, upon the retention of the bismuth in the cecum for more than forty-eight hours. Tenderness over Mc-Burney's point and constipation are common symptoms; the signs of distended or relaxed colon, the gurgling on palpation, and particularly the attacks of pain relieved by posture, when it can be obtained, may suggest abnormal motility of the cecum or typhlatonia. Of the other confusing conditions, the most important are probably disease of the right ovary or tube in women, movable tender kidney regarded by Haussmann as the commonest mistake, and adhesions following appendectomy. Cholelithiasis, pseudo-appendicitis, a very doubtful condition, and colica appendicularis, the correct diagnosis of which most require unusual skill, have also been mentioned by Fischler. The prognosis is usually favorable in the milder forms, at least death does not result, but some of the severer types of obstruction may lead to strangulation, peritonitis, and other grave complications, as in the case reported by Wiemann, and Heiler and Straschenko.

The treatment is by no means definitely determined. Albu believes that internal measures, such as regulation of the diet, laxatives, massage of the abdomen, and prolonged rest, may be

successful. Fischler advises a diet somewhat restricted and carefully adapted to the patient, massage, exercise to strengthen the abdominal muscles and the administration of bismuth, combined, if necessary with magnesia and rhubarb, or, if there is diarrhea, bismuth salicylate may be used. Purgatives and oil and other enemas should be avoided.

The majority of writers, Haussmann, Wilms, Klose, regard surgery as the only satisfactory remedy. The nature of the operation is not settled. Wilms dissects upward a portion of the parietal peritoneum, leaving a pocket into which the cecum is sutured. Rehn and Klose simply attach the cecum to the lateral abdominal wall by sutures, securing a broad area of adhesions. This would seem sufficient in ordinary cases. As in all new operations for chronic conditions, the results are apparently uniformly favorable; at least, none that are unfavorable are reported, although Wilms speaks only in general terms and Klose does not give the final results in all his cases.

I can easily understand why the fixation of the cecum should prevent recurrent attacks of colic, if they are due to temporary obstruction, but it is not clear to me why it should relieve a chronic constipation nor restore the contractibility of an atonic colon, and, therefore, purely upon theoretical grounds, it would seem desirable at the time of the operation to correct all displacements, kinks, or folds that are giving rise, or may in the future give rise, to partial or complete obstruction.

CASE I.—Miss E. H. three years ago complained of feeling in poor condition, sleeping badly, suffering from rumbling and flatus in the bowel. There was habitual constipation, only partly relieved by laxatives. In the past she had had frequent vomiting. On the first examination it was noted that the heart and lungs were normal. There was some tympany on the right side of the abdomen and peristalsis was diminished, but no tenderness was found. Various laxative remedies and diets were tried, and the patient's weight, originally about 130 pounds, increased steadily. Occasionally the cecum was palpable and gurgling was detected, but this was not invariably the case. The sigmoid flexure could also be felt from time to time as a firm cylindrical mass. About two years ago, after the first visit, very distinct tenderness was elicited over McBurney's

point. The ascending colon at this time was distinctly palpable, and was tender upon deep pressure without flinching or rigidity. She underwent then a course of massage, having been assured by the masseuse that her constipation would be relieved. This produced considerable pain in the right side of the abdomen, and occasionally some pain on the left, and the constipation was not improved. The diagnosis of chronic appendicitis was made, and as during this long period of treatment, although the patient had gained in weight, she had never been wholly well, her

Left   Right

Fig. 1.—Case I. Two ounces of bismuth subcarbonate taken at 9 A.M. First exposure same day at 2.15 P.M. Plate shows a greatly distended and ptosed cecum, the lower end of the cecum being below the upper border of the symphysis. Some of the bismuth has also passed into the transverse colon which is lifted by the distended cecum. The bismuth has not quite reached the splenic flexure. There is no bismuth in the stomach and mere traces in the small intestines. Therefore the motility of the stomach and small intestines is normal.

parents requested that an operation be performed. This was done by Dr. Martin in June, 1911. The appendix was free and easily removed, and the postoperative course was entirely normal. For a short time after this she seemed distinctly better, but by August she was as bad as ever, tiring easily and being moderately anemic. The cecum could still be felt, and the lower end seemed to be about the level of the interspinal line. The patient at the last examination was improved somewhat in strength and weight, but the constipation with occasional periods of

relief was practically unimproved. She was therefore referred to Dr. Pancoast for x-ray study. On October 9 two ounces of bismuth subcarbonate in suspension were given at 9 A.M. A picture was taken at 1 P.M., and showed that the stomach was empty and that a considerable amount of bismuth had already passed into the cecum. This confirmed the diagnosis of normal gastric and intestinal motility. On October 11, at 10 A.M., a second picture was taken, and it was found that the cecum still contained a considerable amount of bismuth. It was abnormally long, extending considerably below the interspinal line. There was marked ptosis, with festooning of transverse colon (Figs. 1 and 2).

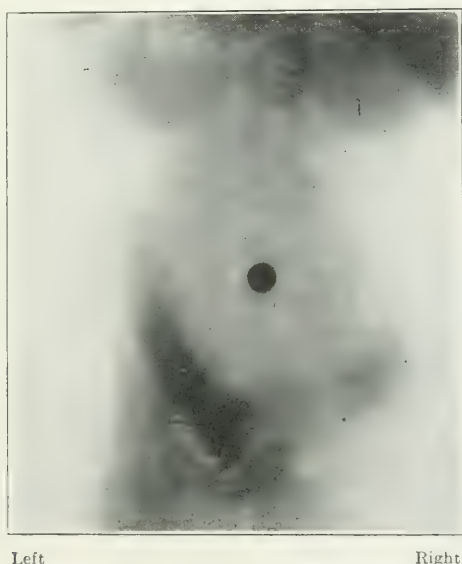Left   Right

Fig. 2.—Case I. Same patient. Picture taken at 9.15 A.M., two days later, without further ingestion of bismuth. There is still a slight accumulation of bismuth in the cecum. The main mass is in the transverse colon.

CASE II.—Miss E. P. was first seen in February, 1908. At this time she was feeling very miserable, and complained of headache and nausea in the morning, dyspnea on exertion, inability to pursue her work, some gas half an hour after eating, and occasional bloating. At the age of twenty she had had an attack diagnosticated as peritonitis. Thirteen years later, when the symptoms had persisted for years, the appendix was removed. Immediately after this operation she developed typhoid fever and was in bed seven weeks. She had always been constipated,

and since the onset of menstruation she has suffered from dysmenorrhea. At this time her weight, 161 pounds, was better than it ever had been previously. She is over six feet tall, however, and appeared poorly nourished. The abdomen was moderately tympanitic; there was considerable splashing in the stomach, and a good deal of tenderness over the right side of the abdomen and hyperthesia in the same region. All the tendon reflexes were greatly exaggerated. The blood pressure was low. The patient stated that the ghost of her appendix had come back to haunt her, because there had been no relief from pain after the operation. The cecum was quite palpable, and from time to time gurgling
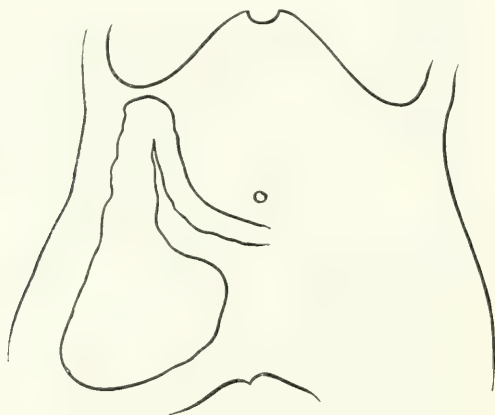

Fig. 3.—Case II. But one plate was taken forty-eight hours after the ingestion of two ounces of bismuth subcarbonate. This plate was not sharp enough for correct reproduction and the outlines of the shadows could only be seen by holding it obliquely to the light. The sketch is an approximate reproduction of the shadow which indicates an enormous dilatation and retention in the cecum. The transverse colon is in good position and shows the permanent results of the Coffey operation done one and one-half years ago.

was present. Considerable relief was given by the application of adhesive straps to relieve the ptosis of the colon, but the constipation was difficult to overcome. The patient slept badly and had vivid dreams. She steadily lost weight, and the marked persistence of the tenderness led finally to the decision to examine the lower end of the colon in order to find out whether adhesions or some other condition could account for her disability. This was done by Dr. Clark who found a few adhesions which he severed and closed the wound. Recovery from the operation was uneventful, but the patient was unimproved. She then decided to spend the winter in Italy, in the hope of overcoming what one of her physicians believed to be a neurasthenic state. Unfortunately, she was

in Sicily at the time of the earthquake, and believes that her failure to improve was due to the excitement of this period. Upon her return a lump developed in the left breast, which was amputated by Dr. George Ross. Microscopic examination showed, however, that the tumor was a simple fibroma. Prolonged rest cure under favorable conditions failed to give any relief; indeed, the patient seemed to be worse, and in view of the profound ptosis of the colon shown by x-rays, it was finally decided, after several consultations, that Dr. Clark should again operate. This he did, resecting a considerable portion of the sigmoid flexure and performing Coffey's operation to relieve festooning of the transverse colon. This operation was only performed at the earnest request of the patient, who was willing to submit to anything in order to regain her health. There was no improvement, and the patient is now apparently a permanent invalid. The diagnosis is not definite, but I can recollect very distinctly at the time of the second and fourth operations, at both of which I was present, the cecum was moved very freely, and was rather long and distinctly distended. This did not attract the attention of any of us at the time, but the history of the case, the prolonged constipation, the failure to improve after the removal of the appendix, the palpable colon, all lead me to conclude that part of her troubles are due to an unfixed cecum. An x-ray picture taken two days after the administration of two ounces of bismuth showed marked retention in the cecum (Fig. 3).

Case III.—M. R. B. was first seen in February, 1908. She was then a girl, aged fifteen years, who had been criminally overworked at school, being occupied from 6 A.M. until 8 P.M., and spending her recesses practising on the piano. As a child she had been well and strong. About the age of thirteen she began to have cramps in the abdomen. These would begin with severe pain in the right lower quadrant, and were sometimes associated with nausea and vomiting. As a rule, the attacks would last for twelve hours, then cease for two or three days. At first they recurred every two or three months, but later increased both in frequency and severity. In the intervals she suffered from a good deal of gas, nausea after food, and occasional vomiting. There was considerable tenderness over McBurney's point, and gurgling upon pressure in the cecum. Peristalsis appeared to be quite active on auscultation. The pulsation of the right common iliac could easily be felt. Patient complained of constipation, which was only relieved by large doses of purgative drugs. She was placed upon a rest cure, during which she gained some weight, but the constipation persisted in spite of all forms of treatment. During this time she seemed extraordinarily listless for a girl of her age, and I ascribed this to anemia, the red cells being 3,280,000. After this she steadily lost weight, going from 93 to 81 pounds. The tenderness in the right lower

quadrant persisted. It was always worse during menstruation, and was supposed to be due to chronic appendicitis that was in part or wholly the cause of the chronic constipation. Finally, appendectomy was done by Dr. Edward Martin. The appendix was free. It showed slight signs of chronic inflammation. Recovery from the operation was prompt and satisfactory. There has been no improvement. The patient at various times has seen specialists in Europe, has undergone a course of osteopathy, and appears practically to have abandoned hope. No *x*-rays have been taken, but the history is typical. An occasional palpable cecum with gurgling suggests very strongly that this was a case in which the movable cecum is accountable for the symptoms.
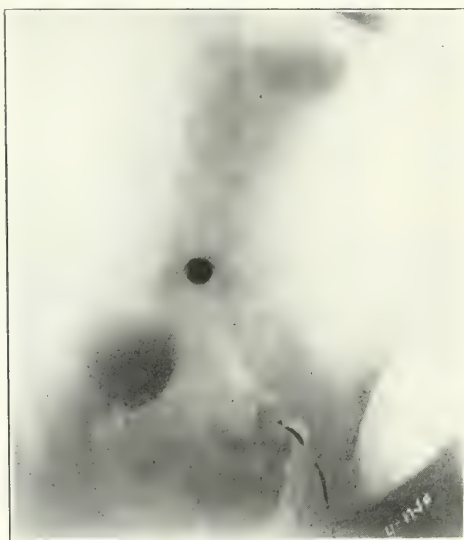
Left   Right

FIG. 4.—Case IV. Bismuth subcarbonate, two ounces, in suspension at 9 A.M. First picture 12.45 P.M. The stomach still contained a large amount of the bismuth which is shown clearly. It is below the umbilicus. The cecum was greatly ptosed and its shadow can be seen extending beneath the ramus of the pubic bone. The bismuth has not distinctly reached the transverse colon.

CASE IV.—Mrs. J. B. P. was referred to me by Dr. W. R. Nicholson. She came complaining of loud gurgling and discomfort in various parts of the abdomen, periods of obstinate constipation alternating with diarrhea, and always much mucus. The appetite was poor. Menstruation was normal. The weight, 105 pounds. The cecum was palpable as a somewhat irregular, freely movable mass containing some small hard

lumps and the lower edge was one inch below the interspinal line. The lower edge of the liver was palpable, but the right kidney and sigmoid flexure could not be felt. This condition has persisted for years. Laxatives seemed to have fairly good results, and the bowel movements became more regular. The appetite was poor, and the weight failed to increase. The cecum continued tender, and there was some diffuse tenderness over the whole of the lower part of the abdomen. There has been no evidence of gastric retention. There was extraordinary improvement for a short time after the application of adhesive straps. Two ounces of bismuth was adminstered, and x-ray pictures taken four and fifty-two hours later. There was no evidence of retention in the stomach or small intestines, but marked evidence of retention in the cecum for a period in excess of forty-eight hours (Figs. 4 and 5).
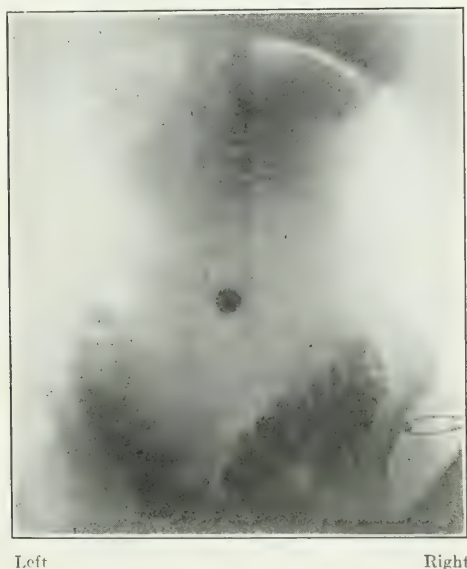

Left   Right

FIG. 5.—Case **IV.** Picture taken at 9 30 A.M two days later. The cecum is still greatly distended with the bismuth and lifts the right side of the transverse colon which is festooned. The dilatation and motility of the cecum and ascending colon and an apparent obstruction at the splenic flexure all seem very distinct.

CASE V.—Miss A. G. C. was referred to me by Dr. Frank Craig. She complained of chronic constipation. Seven years ago she had had a slight attack of pulmonary tuberculosis, from which she had completely recovered. For two years the bowels have moved only after the administration of large doses of purgative medicine, particularly sulphate of
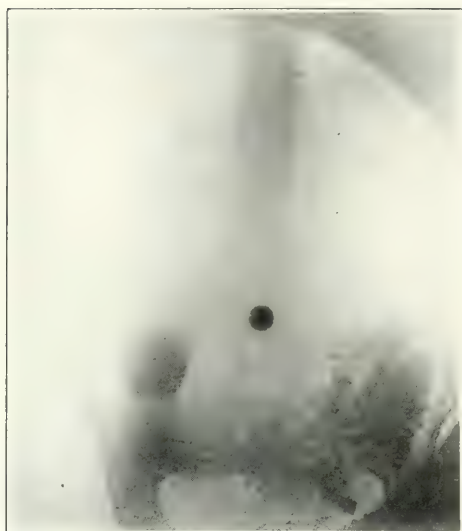
Left   Right

FIG. 6 —Case V. Bismuth taken at 9 A.M First plate at 12.45 P.M. same day Stomach
is ptosed, somewhat sacculated, and lies far to the left and below level of the umbilicus. The
cecum is ptosed and dilated.   There are traces of bismuth in the small intestines and some
has already passed into the transverse colon.

Left   Right

FIG. 7.—Case V. 9.30 A.M. two days later. Cecum is still considerably distended. There
s also apparently considerably distention of the median portion of the transverse colon
Very little of the bismuth has been dischärged.

magnesia. The feces often contain mucus, and sometimes blood. Seven years ago, after treatment for tuberculosis, she weighed 130 pounds. Her present weight is 104 pounds. The thoracic organs are normal. The cecum is distinctly palpable, the lower edge extending half an inch below interspinal line, it moves freely, but there is no gurgling and it is not tender. The sigmoid is palpable. The stomach is ptosed and atonic. Peristalsis is greatly diminished. The right kidney is in the fourth position. The patient was given bismuth and x-ray pictures taken at intervals of four and fifty-two hours. These conformed the physical examination, showing marked retention of bismuth in the cecum and also in the large intestines (Figs. 6 and 7).

No very definite conclusions can be drawn from this study. There seems to be no doubt that many cases are wrongly diagnosticated chronic appendicitis, that in these cases the removal of the appendix is not followed by the relief of the symptom, even if it shows slight signs of inflammation, and, therefore, some other etiological factor must be active. In no less than 3 of the 5 cases I report the appendix had been removed, and in every instance described as the seat of a chronic inflammatory process, and yet in none of those 3 was there any benefit. In 1 of these 3 cases subsequent operations were equally futile.

Although a great deal of work has been done upon the various positions of the colon, the cecum and ascending colon have been, comparatively speaking, neglected. This is due in part to the rather striking displacements of the transverse colon and sigmoid flexure. During the autopsy upon a case of pleural effusion in myocarditis that recently died in my wards at the Philadelphia Hospital, it was found that the cecum was not attached to the abdominal wall until a point midway between its beginning and the hepatic flexure, and that, moreover, the lower end was reflected backward for a distance of two inches and fastened there by adhesions between the two portions of cecal peritoneum that was brought into contact, although superficially it appeared to be normal. This is only mentioned as an illustration of the ease with which these anomalies may be overlooked even by a very competent pathologist. It seems to me likely that the essential lesion in these cases is the atony which results from the partial

and occasional obstruction, and I am inclined to agree with
Fischler that the term typhlatonia is better than cecum mobile,
but the latter appears to be the term adopted by the majority
of writers.

The mere discovery that the cecum is palpable, movable,
and retains bismuth for too long a period should not be regarded
as an adequate explanation for obscure abdominal symptoms
unless all other conditions are excluded, and from the study of
my own cases I am strongly inclined to believe that the dis-
placements of other portions of the colon, the co-existence of a
catarrhal colitis, and possibly an associated chronic appendicitis,
will be of importance in determining the indications for treatment.

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DISCUSSION.

DR. GEORGE E. PFAHLER: I thank Dr. Sailer personally for the
privilege of hearing his paper. He has called attention to a very im-
portant subject, and a condition which I feel that we have overlooked.

I have run across several cases in my examinations by means of the x-rays, and have only happened to recognize the condition when I was studying or looking for adhesions about the appendix. I believe that by the ordinary technique of studying the colon and stomach you would not recognize this condition with any degree of certainty. This, I think, accounts for the statement of one of the authorities that the x-rays are of little use in this field. I see no reason why the x-rays would not demonstrate accurately the condition, not, however, by the ordinary technique. The first examination of the patient should be in the erect posture and then in the Trendelenburg, which would throw the viscera into two different directions, and would permit the free movement of the cecum. In looking for adhesions about the appendix I have done this, and in several cases have recognized the condition. Inasmuch as I have examined only a limited number, I am led to believe that the condition is more common than we have recognized. Now the mere fact that bismuth is retained in the cecum for forty-eight hours, I think we must be slow in accepting as evidence of this condition, because we find this in the majority of cases of constipation. In fact, I think we should be very slow in interpreting the conditions of the colon, because the physiology is not yet worked out and most of the work done on the colon in the human subject has been done in pathological conditions. I surely think that this condition can be demonstrated accurately and positively by the method that I have just mentioned.

DR. ALFRED STENGEL: One feature of the question of movable cecum that has impressed me a good deal is the difficulty of distinguishing between this condition and movable kidney. There are cases, and I have seen a number of them, in which the caput coli could be easily palpated by the method of "gliding palpation," or by moving the palpating hand horizontally over the surface and gradually making more pressure. In this manner the whole caput coli may sometimes be displaced in the direction of movable kidney. In some instances I have found it difficult to determine whether I was dealing with a movable cecum or a movable kidney. The only distinguishing feature that I know of is that in the case of a movable kidney it is possible to get the palpating hand above the upper pole of the kidney, whereas in movable cecum no such possibility exists. It is not altogether easy, however, because in some cases I have found the caput coli twists or moves upward upon an attachment shorter above than below. In other words, the cecum is more movable below, and the caput coli twists over and forward, and gives the sense of an upward pole, which is, in reality, due to the tilt of the caput coli.

Of course, we must recognize, anatomically speaking, that the cecum is always movable. Therefore, a definition of movable cecum is one that

cannot be made absolutely. There is another mode of classification, how-
ever, that I think we ought to consider. It is the method of classification
that we have been forced to with regard to movability of the kidneys,
namely, a classification of a movable kidney which is merely an anatomical
peculiarity, and one which is a clinical condition. The same thing will
apply in the end, I think, to a movable cecum. If we undertook to
rectify every movable kidney that we recognize in clinical examinations,
we should have upon our hands a problem of very great magnitude. In
like manner, if we undertook to rectify this condition—I am speaking
now, not from the basis of any figures, because this is a new condition,
and one which I confess I have recognized only in those grades of severity
which one could not help recognizing—and proceed to treat it surgically,
we would be treating many cases which do not require treatment.

I do not see why Dr. Sailer did not admit the contention that this
condition in itself might lead to constipation. Considering the direction
of the antiperistaltic waves in the large intestine as running toward the
cecum and there meeting with a resistance which sends forward the
direct peristaltic wave, it seems to me easily possible that a movable
cecum might contribute to constipation, and this would naturally be a
symptom of this condition. On the whole, however, it seems to me,
except in the severer grades of mobility, it is very unlikely that this is a
condition of great clinical importance.

Dr. Sailer: It has seemed to me that the method described by Dr.
Klose is not entirely trustworthy, and that there might be conditions in
which the bismuth would remain forty-eight hours in the cecum without
being associated with the anatomical defects which give rise to the cecum
mobile. The method of Dr. Pfahler is probably much better. In regard
to the relation of this condition to chronic constipation I must have
expressed myself badly, but I believe that in the paper there is a definite
statement that constipation is one of the most frequent, if not the pre-
dominant symptom, of cecum mobile.

In regard to the frequency of the disease, there can be at present no
definite statement made. The enthusiasts have found it in a large pro-
portion of their cases. Of course, those who would advocate more con-
servative views have not up to the present time expressed themselves one
way or the other. I have been impressed, as have others, with the unsatis-
factory results obtained in many cases of chronic appendicitis. Therefore,
the real clinical importance of this condition will, I think, be as an indica-
tion for further operative procedures in cases of chronic appendicitis, or
at least in cases of supposed chronic appendicitis where the condition is
due to defects in the cecum, not inflammatory, but merely structural.

DESCRIPTION OF A SERIES OF FRONTAL AND SAGITTAL SECTIONS OF THE ADULT HUMAN HEAD RECENTLY ACQUIRED BY THE MÜTTER MUSEUM.[1]

By JOSEPH P. TUNIS, M.D.

As I have had the opportunity of preparing these sections, I have also been asked to give a description of them. The method of preparation is a simple one, which I have already described in the *Anatomical Record* for February, 1909.[2]

The sections are for the most part about an inch in thickness. They are in two series, in one of which the saw cuts were made in a frontal or transverse direction and in the other in a sagittal direction. Of the former, there are six sections from the head of a young white woman, aged about twenty-seven years. The other head, of a white adult male, was divided in a sagittal direction, or from before backward, into five parts. From these two heads there are sixteen surfaces which are of anatomical interest, and which I propose to describe briefly, laying special stress upon the anatomical points of the brain which are demonstrated thereby. The principal feature of the method of preparation already mentioned is that while the frozen sections were still frozen they were polished on a rapidly revolving wooden wheel wet with cold water and finely divided pumice stone. The surfaces are in this way rendered clear cut and give a much better demonstration than if they were not polished.

Of these surfaces I have prepared sixteen photographs with leaders attached to the most important anatomical points. For their better preparation these photographs have been covered with glass and passe-partouted. Every surface was photographed and described in this way, except two which belong to practically unimportant fragments.

In my series of eighteen lantern slides, which I now have the pleasure of showing you, even these two fragments have not been overlooked, although practically the surfaces in question are identical with the surfaces with which they came in contact. In all, there are more than one hundred and twenty-five anatomical points demonstrable by these sections.

As examples of what these sections show I have had two of the figures reproduced in the accompanying figures. Fig. 1 represents a cross-section of head No. 1, and this particular surface represents Section 4 of this series. At the first glance one is impressed with the asymmetry of the brain which seems to be better developed on the right side than on the left. In this head I was fortunate in securing a comparatively fresh brain, which on sectioning appears in close relation to the meninges and skull. In Fig. 1 there are two points which are of special interest, namely: (1) The condition of the internal capsule and of the apparent division of the lenticular nucleus into three compartments. (2) The division of the external auditory meatus in such a way as to show a perpendicular section of the drum membrane and its relation to the attic. Also the cartilaginous interspaces first described by Santorini are well shown.

In Fig. 2 the median sagittal section of head No. 2 is shown. In this one is impressed by the enormous intradural hemorrhage which has so permeated the specimen as to render the exposed surface less distinct than it is in Fig. 1. While I might dwell upon a number of anatomical points described by similar photographs among the sixteen already referred to these two will serve as examples.
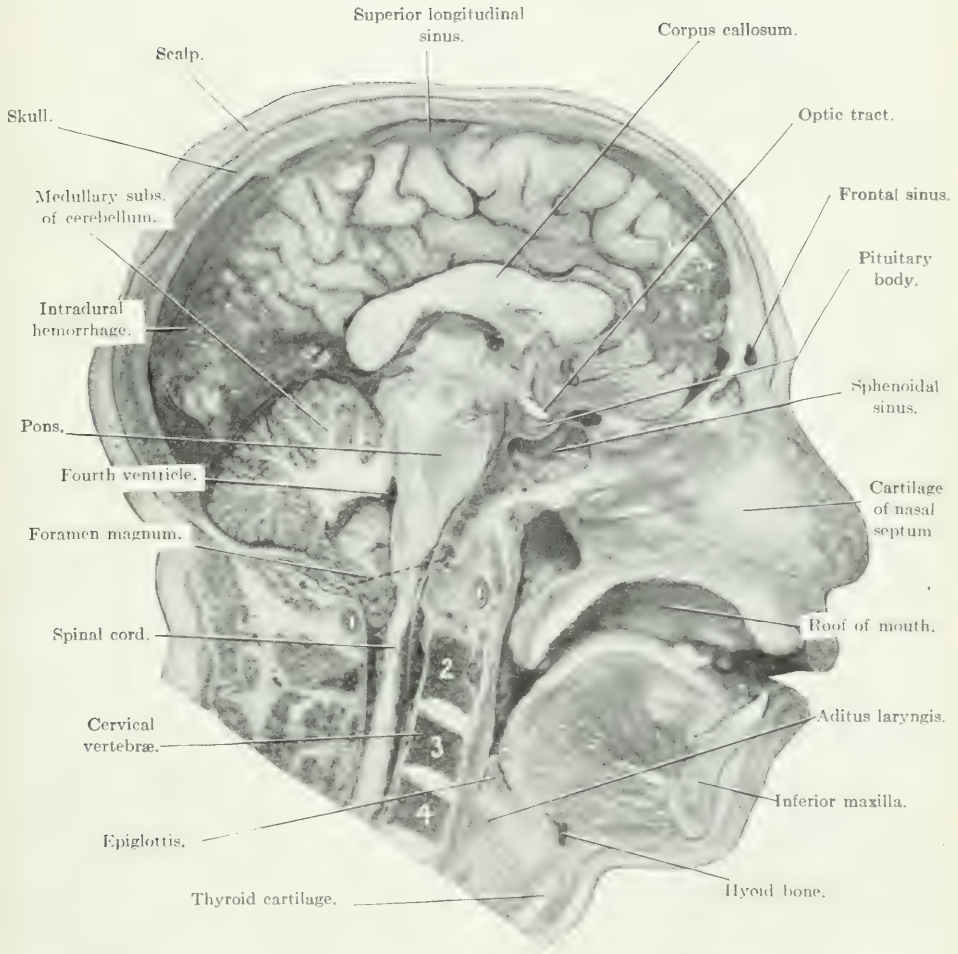
FIG. 1
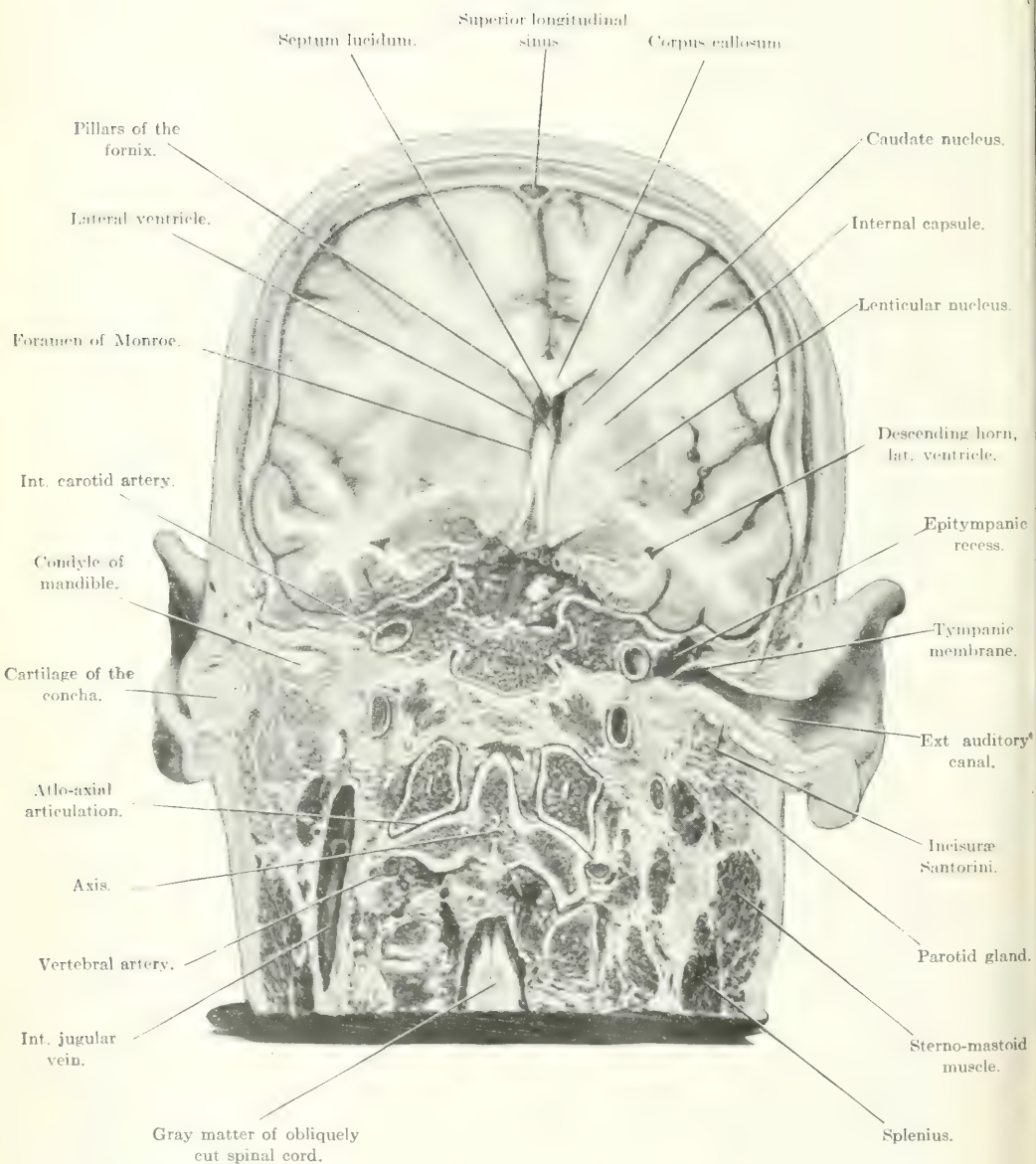
Anterior view of section No. 4. In addition to the structures of the brain, seen on cross-section near its middle, a number of interesting anatomical points are demonstrated in relation to the ear.

Prepared by Dr. J. P. Tunis.

Fig. 2

Superior longitudinal sinus.

Corpus callosum.

Scalp.

Optic tract.

Skull.

Medullary subs. of cerebellum.

Frontal sinus.

Pituitary body.

Intradural hemorrhage.

Sphenoidal sinus.

Pons.

Fourth ventricle.

Cartilage of nasal septum

Foramen magnum.

Spinal cord.

Roof of mouth.

Cervical vertebræ.

Aditus laryngis.

Inferior maxilla.

Epiglottis.

Thyroid cartilage.

Hyoid bone.

Sagittal section showing the left side of a head with the nasal septum almost intact. The cervical vertebræ have been numbered from above downward. The interior of the larynx lies a quarter of an inch below the surface.

Prepared by Dr. J. P. Tunis.

DISCUSSION.

DR. GEORGE McCLELLAN: The preparations which Dr. Tunis has made for the Mütter Museum have been shown this evening at my request. The excellence of these preparations must be apparent to all of you. I have only to remark that sections of the various regions of the body, showing the approximate relations of the structures thus revealed, are always interesting and often instructive; but in regard to the other regions than that of the head there must be some allowances made for the effect of freezing, which is very apt to produce a change in the normal relations. On the head, however, owing to the skull, the effect of atmospheric pressure, often also a distinguishing factor, is eliminated; hence, the value of the sections which Dr. Tunis has so admirably accomplished. I have seen a great many sections and have been interested in them always, but I do not know of any which have the excellence of these of Dr. Tunis, and I consider that we are fortunate to have among our Fellows of the College one whose skill and workmanship have produced these results. The illustrative photographs with their clear references are most admirable. The work is entirely original as far as I know. As chairman of the committee on Mütter Museum I consider that we have a most valuable acquisition in this collection.

THE TREATMENT OF MELENA NEONATORUM BY HUMAN BLOOD SERUM.[1]

By WILLIAM R. NICHOLSON, Ph.B., M.D.,

GYNECOLOGIST TO THE POLYCLINIC HOSPITAL, PHILADELPHIA; ASSOCIATE IN OBSTETRICS, UNIVERSITY OF PENNSYLVANIA.

WHILE the word melena forms an integral part of the title of this paper, it is to be understood that it is used out of respect alone for its position in a nomenclature which is scientifically a thing of the past. The type of case, the subject of this communication, does sometimes show this symptom, melena, as a major manifestation, but more often as only a very minor one. Possibly it would be more exact to give the title hemorrhagic disease or diathesis to this symptom complex, but it is to be remembered in forming one's conception of the matter that the general symptom hemorrhage may be but a minor expression of this diseased condition during life, and in fact that it may be entirely absent clinically, only appearing upon postmortem examination.

The clinical picture presented by these cases is most striking. The insidiousness of onset it is true is often diagnostically deceptive, but the rapid development of grave symptoms soon banishes any attempt to belittle the condition of affairs. Strangely enough the babies who have developed this diseased condition have almost without exception in our experience been most beautiful specimens at birth, normal or above in both weight and strength. It may also be noted in passing that the labors in the vast majority of these cases have been easy.

A few days after birth, however, it is observed that the child has some slight temperature; the stools are also of a faulty color,

either being dark green or containing blood, which may be either occult or frank. A papular eruption is to be found in a large proportion of the cases as a rather early symptom, and this may afterward become a true hemorrhage into the subcuticular tissue. Anorexia, vomiting, and indeterminate nervous symptoms are also of course in evidence, and in a large number of the cases bleedings from various parts of the body make their appearance. Any or all of the mucous and serous membranes may be the site of this hemorrhage.

The most usual sites of bleeding are the skin, as has been mentioned, the cord or umbilical ulcer, the vagina, the bowel, and, as in one instance of the writer's, the mucosa of the alimentary tract high up, the blood flowing from the mouth of this child in a steady little stream. Keeping pace with these alarming symptoms there is a progressive emaciation and weakness, which in a period of no more than forty-eight hours changes the child from a condition of exuberant health to that of extreme malnutrition.

In the experience of the writer, comprising about a dozen cases, there has been no benefit from any form of treatment except in the one case to be reported. With the just-mentioned case as an exception all the other babies have died within a week of the onset of symptoms. The writer's mortality has therefore been 100 per cent., and this in general has been the experience of most other observers, at least until within a very recent period. DeLestre reports a few cures by the withdrawal of a small amount of blood, and Cope, working under Hamill, has in one instance seen the same remarkable result. In general, however, the prognosis has been considered practically hopeless.

As yet there is no etiology established with certainty. In former times when Buhl's and Winckel's diseases were considered pathological entities the way seemed plain enough. Syphilis, cerebral injuries, hemophilia, etc., were confidently believed to be the causes of this condition, and the spirit of investigation was stilled. A little later, however, this confidence began to weaken, and the same diseased conditions were not considered

as truly causative, but simply as predisposing factors, while at the present day all consideration has been withdrawn from them as in any way concerned, since anyone having experience with the manifestation of pathology which we are considering will be impressed by the fact that in the large proportion of the cases the children are particularly healthy at birth. To the writer's mind the preponderance of probability tends toward an explanation in which septic infection plays the true initial role, the blood changes and other manifestations varying as they do more or less with each case, being simply expressions of different varieties or doses of poison. This theory, while it does not explain all the manifestations, and while there are links in the evidential chain yet to be supplied, seems to fit the clinical picture better than does the theory of a congenital maldevelopment of the blood chemistry, for the reason that while it is perfectly conceivable that a healthy child may receive a fatal dose of infection during or soon after birth it is hardly to be imagined that a baby with a congenital blood disease of whatever nature could develop *in utero* to perfect maturity and yet within a few days develop a disease which in spite of all treatment progresses rapidly to a fatal issue.

To say that the complement is lacking or that thrombokinase or prethrombin is at fault is not to express a true etiology, since, as has been said it, is not conceivable that a child can develop *in utero* to perfection, it being as dependent for its health upon its blood before birth as in after life, and yet within a few hours or days after the inception of extrauterine existence, and without any cause operating *de novo*, show such a calamitous pathological outbreak as the condition under discussion. On the other hand, if it be granted (it is admitted freely that it is not as yet proved) that septic infection is the fundamental pathological factor, the changes in the blood chemistry may by analogy be explained on the basis of the operability of various toxins.

Believing as I do that the blood changes, chemical and otherwise, are the results of a primary sepsis in at least a large proportion of these cases, it is natural that the avenue and source

of this infection should be considered. As to the avenue of the infection it does not seem to the writer that it is justifiable to lay the blame upon the cord with the frequency usual to those considering this subject. Anyone who is accustomed to inspect the stump of the umbilical cord and the ulcer left after its fall will realize how general are the conditions in perfectly healthy babies, upon which some investigators have laid stress, as being the evidence of a pathological change. In other words, there is constantly moisture, some peripheral redness, and if very strict cleanliness has not been observed in the care of the child, quite a little odor. Moreover, if one will realize (1) how difficult it always is to infect granulating tissue, (2) that after a ligature has been applied infection through the exposed end of the cord is impossible, and (3) that the children usually die before the cord has had time to fall, it will at least seem reasonable to demand stronger proof of cord infection than has so far been produced, and to continue in the belief that the usual mode of entrance is by some other avenue. From the fact that in probably the large majority of these cases there is marked primary involvement of the gastro-intestinal tract, and, moreover, that this tract is the one avenue through which infection may enter with the greatest ease, it has been for years the belief of the writer that this tract offered the usual way of approach, and in accordance with this belief he has, in so far as it has been possible to him, excluded the so-called mouth cleansing after birth from his hospital services and private work, since he has been convinced that far more chance is given for the introduction of organisms by this attempt than for their removal, even if they are there to be removed.

One other point is felt of sufficient importance to be mentioned, namely, that while in older times these infections were more common in maternity hospitals, as a matter of fact the writer has seen several cases in private work, while they have almost disappeared from his hospital services. It may be that the introduction of the steam sterilized baby bath-tub, together with the greater care in handling young infants, has decreased

markedly the incidence of the condition in hospitals. Several cases reported in a previous communication occurred in an institution in which no such care was possible, the needful facilities being lacking. It is to be remembered, however, that the dangers incident to the first few days of life in a hospital nursery are absent in private practice, in so far as they are dependent upon the transference of infection from one child to another, and yet these cases occur today in private work. This being so, it would seem to the writer that the evidence bears out the belief previously expressed that it is an infection by the mouth, and further, that such infection occurs in the maternal birth canal. It is a matter of common knowledge that the lower part of the genital tract is rich in organismal life, and further that the head often remains stationary in the lower vagina for a considerable time. Moreover, in a certain percentage of cases, through interference with the placental circulation, the infant attempts to inspire while the head is still in the vagina; this is evidenced by the sudden imperfect extension of the head in the absence of a pain and is quite frequently noticed. It is the opinion of the writer in view of these facts that prophylaxis of many of these cases is impossible except in so far as prompt delivery may serve.

The recovery of the case now to be reported, the said recovery being undoubtedly due to injections of blood serum, has greatly impressed me. The details of the case are as follows:

Baby M. C. M. was delivered at full term. The parents were both healthy. The labor was normal and progressed rather rapidly until the head of the child was in sight on the perineum. Slight delay occurred at this point, but the retardation was in no sense unusual, and we were confidently awaiting spontaneous delivery when suddenly there was a copious discharge of meconium alongside the child's head. This was believed to be due to the interference with fetal circulation caused by the increased frequency of the uterine pains, which, as has been noted, had been for a time unavailing. Forceps were accordingly applied at once, and the child was rapidly extracted in a moderate asphyxia and fairly plastered with meconium. The convalescence of the

mother was uneventful throughout. The child, a particularly fat and strong baby, did well until the fourth day, except that it had a slight elevation of temperature, it being over 101° all the third day and reaching 102° on the morning of the fourth. The stools also continued dark, but at this period they were simply meconium. On the morning of the fourth day a papulo-squamous eruption was noticed on the chin. The characteristics of this rash may be appreciated by the fact that the nurse believed it to be due to irritation, but careful inspection based on previous experience did not enable me to take this comforting view. Aside from this, and the fact that there was the before-mentioned temperature, a symptom not unusual in newborn babies, there was nothing to cause foreboding at this time except that the child did not look as well as it had done previously; but I left her feeling far from comfortable, and was not at all surprised to be called back within an hour because of bleeding from the cord. Inspection showed that the blood came not from the mummified distal end of the cord, but from its periphery, just external to the abdominal insertion. Adrenalin and pressure having failed, a ligature was passed by needle through the cord just within the abdominal wall, which checked the bleeding entirely. The diagnosis was established, however, to my mind, and corroboration was furnished by the occurrence of vaginal and some rectal bleeding later on the same day. Slight traces of blood in the vomitus and a hematoma under the left lateroposterior neck muscles followed within the next two days. The emaciation progressed even more rapidly, it seemed to me, than is usual in these cases, and was associated with decided cervical retraction and restlessness. The child also seemed hyperesthetic all over its body, crying whenever it was touched, its tongue was dry, and its general appearance caused the most grave apprehension.

As a forlorn hope, in fact without any real belief that any good would result, I determined to try the injection of normal human blood serum. I had read the articles which appeared some two years ago by Dr. Welch, and with the most unbounded skepticism I made arrangements with Dr. Dorrance to procure a speci-

men. In passing I would like to remark, in order to emphasize the wonderful change that subsequently occurred in this child, that when Dr. Dorrance first saw her, on the occasion of the first injection, he felt that it was most foolish to interfere with what to both of us seemed to be her manifest destiny. In the emergency we were compelled to use the father as the donor for the first injection. A little more than 20 c.c. were injected into the tissue of the back. The next day 18 c.c. were injected in the morning and 10 c.c. at night. On the next day there was vaginal bleeding, but only 6 c.c. were injected, as our supply was temporarily low. The following day the cord separated in a perfectly normal manner; there had been no bleeding externally during the night, but the neck was discolored and swollen. Two doses were given on this day, the morning measuring 18 c.c. and the evening 14 c.c. Upon this same day a small swelling, which we believed to be a cephalhematoma, made its appearance. The next day the first normal stool was passed. The baby was evidently improving, and but 6 c.c. of serum were administered. A supply was kept in readiness for a couple of days, but was not used, as the child was free from any sign of active bleeding and the hematoma was decreasing in size. The weight was also increasing, and the temperature remained normal. I have had the pleasure of seeing this child within the last two weeks, and she is a large, healthy girl, presenting no evidence of the severe illness just recorded.

There is one point which I think would be well to emphasize in passing, namely, that as soon as the child showed symptoms of the diseased condition it was immediately placed upon artificial feeding. This I consider the proper thing to do in all cases of severe illness within the first few days of life, not only for the reason that the maternal supply at this period is so scanty, but also because I believe that injurious maternal milk is not as rare a commodity as some seem to believe.

The method of giving the injections is simplicity itself. Before considering it in detail I would mention that it has a distinct advantage over actual transfusion, which has been suggested

and performed by some to meet the same indications, for two reasons: (1) That the latter requires special skill for its performance, it being a delicate operation even in the adult and requiring a few special appliances; and (2) that while there is never any difficulty to obtain donors of serum, on the other hand, thanks to the untiring efforts of the ever-present newspaper reporter, the public looks rather askance at requests for donors in actual blood transfusion.   In the case just reported this difference was made very evident by the increase in the choice of donors which was afforded us after they were assured that they would simply have to submit to an old-fashioned bloodletting.

One word as to the method employed.   Dr. Welch removes the blood from the vein by aspiration, and this procedure, while requiring a little training and a small amount of special apparatus, is without doubt better than that used by us in this instance. Being unprepared and face to face with a distinct emergency, we simply incised the skin after careful cleansing, and collecting the blood by gravity we allowed the serum to separate spontaneously from the clot.   With an ordinary antitoxin syringe the injection was made into the back of the child anywhere from its scapulæ to its buttocks.

Small quarter-liter flasks were found to give relatively the largest amount of serum, and by using this size it is not necessary to place them in an inclined position while the serum is separating.

From my experience with the overwhelming mortality of this condition under expectant or any rational plan of treatment, the outcome of this case impressed me at the time as verging on the miraculous.   I have no doubt that a fatal result was averted by the injections of normal human serum, and I am led to hope that in this very simple therapeutic measure, which is always ready to the hand of even the isolated practitioner, we may find ourselves in possession of an agent which will be found potent for good in combating diseased conditions before which we have in times past confessed defeat.

NORMAL HUMAN BLOOD SERUM INJECTIONS IN MELENA NEONATORUM AND OTHER CONDITIONS.[1]

By J. E. WELCH, M.D.,

NEW YORK.

APPROXIMATELY eighteen years of trial to which the serum of the horse, immunized artificially against the toxin of diphtheria, has been subjected has put it in the rank of a specific in the treatment of diphtheria. The principle of artificial immunization operative in connection with this serum has been adopted in other instances, so that now we have other antitoxic sera, more or less efficient, developed against several organisms. In the meantime, during the growth of knowledge concerning the curative properties of the serum of animals artificially immunized, it has been learned that normal sera possess under certain circumstances a decided therapeutic value.

Those experienced in the use of the various sera are well aware that their advantages are not unalloyed. Associated with the brilliant successes attending their use are numerous tragedies, begotten of their untoward effects. These effects are very commonly encountered when the serum of an animal is used in a different species, but fortunately are rarely severe enough to produce death, and they do not occur when the serum of the same species is used. This latter observation I made in 1902, in using normal human blood serum after having had a disagreeable experience with the use of diphtheria antitoxin.

A young man, aged twenty years, ill with pulmonary tuberculosis, was admitted to the New York City Hospital. After

a fair trial of the then recognized methods of treatment, I suggested to the attending physician that we withdraw a quantity of blood from some person convalescing from a surgical condition, which had not in any way affected the quality of the blood, allow it to clot, and with the separated serum inject our tuberculous patient, having in mind the possibility of furnishing some disease-resisting substance which had prevented the donor from contracting tuberculosis. The proposition seemed impracticable at the time, and a substitution was made. It was decided to use normal horse serum instead. This also was not procurable, but a substitute was furnished by Dr. William H. Park, in the form of a low-grade diphtheria antitoxin, having a strength of 150 units. It was reasoned at the time that the antitoxic properties of the serum, which was elaborated specifically against the diphtheria toxin, would also neutralize the toxins of other infectious diseases, a view then quite commonly held.

Following directions, I began subcutaneous injections of the weak antitoxin; 10 c.c. were given three times per day. At the end of twenty-four hours there was a notable change in our patient, but not for the better. He complained of severe headache and excruciating pains in the joints, especially in the knees. The temperature, which had been quite constantly about 102°, rose to above 104°, the respirations increased, and there appeared over the entire body the worst itching, burning, urticarial rash I have ever seen. A few more injections were given, and with each the symptoms grew worse, making it necessary at the end of the second day to discontinue the treatment. The injections made our patient worse than he had been—in fact, he never regained the loss induced by the antitoxic serum injections.

Shortly after this experience I succeeded in getting from some of my patients a small amount of normal human blood serum, and made subcutaneous injections in pneumonia, typhoid fever, erysipelas, and diabetes. The disagreeable experience I had had with the diphtheria antitoxin injections made me overcautious, so that I used of the normal human serum at each dose from 1 to 3 c.c. I made no distinction between the alien and homo-

logous serum. My experience with the larger doses of low-grade antitoxin made me fear untoward symptoms from the human serum, therefore, the very small doses were used. Boldness begotten of uniform absence of symptoms following single and repeated injections of small doses of normal human blood serum has led to an increase in the size of the dose. From time to time the amount has been increased, until I am now ready to state that normal human serum in doses of 300 c.c., administered subcutaneously, or repeated in smaller amounts over a period of nine months, to the amount of 3500 c.c., will not cause any of the symptoms so often produced by single or repeated injections of a foreign serum.

Since the beginning of the use of antitoxin the untoward symptoms have been occasionally fatal and are so frequently met with that they have instilled a fear into many of the profession and the laity. These symptoms appearing after single or repeated injections of alien serum are now known respectively as "serum sickness" and "anaphylaxis." The literature descriptive of the research on this subject is so voluminous as to render a review impossible. Probably every research laboratory in existence has in the past directed, or is at present directing, efforts toward discovering the nature of the sensitizing body, or is endeavoring to discover some substance which will neutralize the sensitizing body. In a recent volume of *Ergebnisse der Allgemeinen Pathologie*, which reviews this literature to 1910, four hundred and twenty-two contributions are referred to which deal with this subject.

From all of this study of anaphylaxis have come some very important observations. Those perhaps of most importance and which should be very seriously considered when the giving of alien serum is proposed as a therapeutic agent, are three in number.

Biedl, Kraus, Arthus, and others have demonstrated that a marked fall in blood-pressure accompanies anaphylactic shock. These authors have also demonstrated that the coagulation time of the blood is considerably lengthened in this condition.

The third and most important change brought about is a decrease in the quantity of complement in the blood, which has been proved by Michaelis, Fleischman, Friedmann, Friedeberger, Hartoch, Scott, and others.

Nutritional experiments, dealing with injections of alien serum into guinea-pigs, have proved that it causes either a retarding of growth or death of these animals. Reviewing, then, in a few words, the effect of subcutaneous injections of alien serum, we have the following:

1. Serum sickness with its fever, disturbing urticaria, joint pains, dyspnea, albuminuria, hematuria, and occasionally sudden death.

2. It reduces blood pressure.

3. It decreases the coagulability of the blood.

4. It causes a reduction in the amount of complement.

5. It interfers with nutrition.

Subcutaneous injections of homologous serum do not produce the above conditions. In my own experience with the use of normal human serum I have never met with any untoward effects.

For the sake of comparing the nutritional effect of homologous with alien serum, an experimental study with normal human blood serum was made. The subject of the trial was a premature infant, born at about the eighth month of gestation. He took nourishment by mouth badly and steadily declined in weight from 2025 grams, the weight at birth, August 17, to 1625 grams, September 5, a loss of 400 grams in nineteen days. On September 5, injections of normal human serum were begun and were continued through twenty-one days, to September 26. The baby's food remaining the same as previously, the weight began immediately to increase, and, suffering slight fluctuations, gained steadily for fifteen days to 2200 grams, a gain of 575 grams. It then receded during the next six days to 2125 grams, which was 100 grams more than the weight at birth. During this period the child received daily subcutaneous injections of normal human serum, in amounts varying from 20 to 78 c.c., receiving a total

of 896 c.c. in twenty-one days. At this time the child was taken away in good condition and able to nurse well.

Of other conditions in which I have had experience in the use of normal human blood serum the various bleeding conditions rank first, and of these, more especially the hemorrhages of the newborn. Experience to date, which I have had with 32 of these cases, now warrants a few conclusions.

The infrequency of this disease and the rapidity with which it proves fatal make it extremely desirable that we have a well-known specific, easily obtainable, with which to combat it. The beginning of this condition is not always in the same way. The baby may be in every way apparently healthy, plump, rosy, and functionating normally. Without warning it may vomit a quantity of fresh blood or pass bloody or tarry stools, and these may be the only manifestations of hemorrhage. The bleeding may be subcutaneous, of a petechial nature, or occur as hematomata. The umbilical stump, a divided prepuce, or the gums may be the sites of hemorrhage. Fatal internal hemorrhages not infrequently occur without external manifestation and may affect the brain or any of the thoracic or abdominal organs. These cases clinically may show icterus, or may simply grow pale, feeble, and die without apparent adequate cause. The autopsy makes the diagnosis, and we find the hemorrhages usually within the serous cavities or beneath a serous membrane, such as the pulmonary pleura, in the pericardium, under the capsule of the liver, under the kidney capsule, or in the peritoneal cavity. Microscopic examination of the various organs taken at autopsy shows anemia and cloudy swelling of the epithelium of the parenchymatous organs. The epithelium of the gastro-intestinal tract usually shows the most advanced changes of degeneration and desquamation.

Drawing a conclusion from experience with 32 cases of hemorrhagic conditions, treated by normal human blood serum, I am convinced that this agent is a specific for this pathological condition. For a partial detailed report on 13 of these cases I refer you to the June, 1910, issue of the *American Journal of the*

Medical Sciences. Time does not permit a review of the cases not reported, but I will review briefly a few of them; others would be but a repetition:

B. Z., male child, delivered at 9 P.M., October 19. At 9 P.M., October 20, vomited blood; at 11 and 12 P.M. bloody passages. October 21, bloody passages at 3 A.M. and 4 P.M.; October 22, bloody passages at 4 P.M.; October 23, bloody passages at 11 A.M. and 4 P.M.; October, three passages free from blood.

Normal human blood serum was injected as follows: October 21, twenty-four hours after bleeding began, 112 c.c.; October 22, 54 c.c.; October 23, 19 c.c.; October 24, 12 c.c.; October 25, 10 c.c.

When born this child did not have the plump, rounded contours of a normal baby, but appeared poorly nourished. The stools were from the beginning very foul-smelling. The first temperature, taken twenty-four hours after birth, was $100\frac{4}{5}°$. On the next day it rose to 103°, and fluctuated between 100° and 103° for a few days, when it returned to normal. When the serum injections were begun the child was too weak to nurse and cried but feebly. Within twenty-four hours after the first injection he was able to nurse his mother, cry more vigorously, and made a steady gain to a normal condition.

N. J. L., born June 10th; second child; negative family history; first child stillborn on account of difficult labor. Present labor lasted two and one-half hours; breech presentation; no interference; no anesthesia; weight at birth five pounds, twelve ounces. Child appeared normal, and cried lustily; no cyanosis. On the third day it was slightly jaundiced. At this time it was noted he had a peculiar cry, there were spasmodic muscular movements, and he stopped nursing. There was no vomiting; the stools became yellow and were normal. Physical examination showed a small child with skin wrinkled, cyanotic and dusky. He was aroused with difficulty, occasionally giving a loud, shrill cry when disturbed. The fontanels were noticed to be tense and bulging. The pupils were slightly unequal, and the eyes were turned to one side at intervals. There was rigidity of the neck

and extremities at intervals. There was twitching of the muscles of the face, arms, and legs. The knee-jerks were exaggerated He would not take the breast, but would occasionally swallow fluid administered with a dropper. There were no evidences of hemorrhages into the skin or elsewhere. Lumbar puncture showed increased pressure, and one-half ounce of bright red fluid was withdrawn, which contained 5,100,000 red cells, 2400 leukocytes, and 90 per cent. hemoglobin. The specimen appeared to be pure blood and would not coagulate. The bulging of the fontanels disappeared at the time of the puncture, but returned fifteen minutes later. Sixty hours after the onset of the first symptoms treatment by normal human blood serum was begun. During this time the condition of the child became progressively worse, so that during the last twenty-four hours, he could not be aroused at all, ceased to swllow, and the lack of nourishment and loss of fluid gave him the atrophic appearance of athrepsia.

He was not weighed on account of his poor condition. At this time 30 c.c. of serum were given subcutaneously; six hours later 30 c.c. more. After the second dose the child began to show improvement. He appeared brighter and was able to nurse, and the muscular twitching was less marked. Sixty cubic centimeters more serum was given in this twenty-four hours, at the end of which time the twitching had ceased entirely and he was nursing regularly every two hours. At the end of the second twenty-four hours the fontanels were still bulging and another lumbar puncture was done, drawing off one-half ounce of blood-tinged spinal fluid, showing that active hemorrhage had ceased. Serum administration was continued for five days, the amount being diminished each day. In seven days this baby received a total of 630 c.c. administered in twenty-three doses. Improvement was continuous. At the fourth week he had regained his original birth weight. At two months he weighed 8 pounds 8 ounces; at three months 12 pounds; at four months 15 pounds. At four months he appeared to be a normal child, having no spasticity; he held his head up, was able to hold objects in his hands, smiled upon provocation, and did not show

signs of mental insufficiency.   Today he is a normal baby, one year and six months old.

B. A., the third child, a male, aged five and one-half years, had always been very healthy until the present trouble. One afternoon he received a slight blow on the abdomen from the handle of his bicycle. Following this there was a very large hemorrhage under the skin. A few days later he fell ill with tonsillitis, which lasted four or five days. While convalescing from this attack he had frequent hemorrhages from the nose and some oozing from the gums. About ten days later, on July 10th, the epistaxis was very marked; the child vomited a large quantity of blood and passed large bloody stools. The epistaxis and bleeding from the gums continued throughout the 11th. On the morning of July 12th a large quantity of blood was again vomited and many bloody stools passed. On the morning of the 13th again vomiting of blood and bloody stools. At this time I was called to see the child and found him very pale, tossing about the bed with air hunger, and so pale the lips were of a color indistinguishable from that of the skin surface. The temperature at this time was 103°, pulse 140, respiration 48. Between 12 o'clock noon and 12 o'clock midnight the child received 240 c.c. of normal human blood serum. July 14th there was a very slight hemorrhage from the nose, and some disintegrated blood passed in the stools. After this there was no more bleeding. The serum injections were continued, however, for five days, at the end of which time a total of 1034 c.c. had been administered hypodermically. After this the child made a slow but steady recovery to its normal condition.

L. M., male child, aged ten years. His mother was subject to severe and almost uncontrollable hemorrhages. Patient himself in the past had been subject to prolonged and almost uncontrollable hemorrhages from slight wounds. He was admitted to the Fordham Hospital after having fallen and punctured two wounds in the anterior part of the tongue with his teeth. On admission the tongue was swollen and black, and was bleeding steadily from two small puncture wounds near the tip. For the

first twenty-four hours he was given calcium lactate gr. 10 q. 4 h.,
and adrenalin solution to the tongue on cotton in the form of
a wet dressing.   Bleeding was continuous.   Peroxide of hydrogen
was applied locally as a wet dressing; bleeding continued.   Next
day vomited a large clot of blood.   Compresses of gelatin solution
were applied locally and changed every hour through the night;
bleeding continued.   Treatment with gelatin, adrenalin, peroxide,
and gr. 10 calcium lactate q. 4 h. was continued for four days
without the slightest effect.   On the fifth day a local dressing
of fresh beef serum was made and changed frequently without
the slightest effect.   On the sixth day one ounce of normal
human blood serum was injected subcutaneously.   The hemor-
rhage stopped within four hours after receiving the serum and
did not return again.   The boy was discharged on the fourteenth
day very anemic, but with no tendency to hemorrhages.

I. J. G., whom I saw in consultation with Dr. Dowd, was a
young man, aged twenty-nine years.   His family and personal
history were negative.   It was noted by his family and friends
that he was always very pale but perfectly well nourished and
healthy.   Without warning his nose began to bleed and could
not be stopped.   After he had bled about a pint, according to
the family estimate, Dr. Dowd was called.   The nose was packed
very tightly from both front and back, but without effect, as the
blood lampwicked through the packing and continued to drip.
The packing was removed several times and replaced tighter
each time, but still without effect.   The hemorrhage reduced
his hemoglobin to 65 per cent. and red blood cells to 2,000,000.
On the fourth day I began injections of normal human blood
serum, and within thirty-six hours the bleeding had stopped and
did not return.

The underlying condition in these bleeding cases I believe
has to do with the endothelium lining the bloodvessels, and I
think a disturbance in the balance of the ferments of these cells
is the immediate cause of the hemorrhages.   This disturbance I
believe to be due to malnutrition.   The malnutrition may be
caused in different ways, but in the end has the same result.

In the bleeding babies we find marked putrefaction, hyper-secretion of mucus, and malodors indicative of marked decomposition in the colon. This decomposition is accompanied by the production of toxins, which are absorbed and interfere with the nutrition of the endothelium, possibly by producing a cloudy swelling, and thereby upset the balance normally maintained between the ferments and antiferments of these cells. In a very recent case of hemorrhage in the newborn a foul odor, identical with that of the stool, was exhaled from the general skin surface. Hemorrhages so commonly reported in specific babies can be accounted for in this way, and also those occurring in individuals having a bacteremia. The toxins of these various conditions are equally capable of destroying the normal equilibrium of the endothelium.

A long list of observations have descended to us from the literature which seem to have well established that these hemorrhages are due to some abnormal condition of the blood itself, that it is a blood disease. The main facts in support of this conclusion are the delayed coagulation time of the blood and what appears to be a hereditary tendency. In an article entitled "The Relation of the Blood Platelets to Hemorrhagic Disease," Dr. W. W. Duke has pointed out that there is a marked diminution of the blood plates in these hemorrhagic conditions, and that when these are supplied by transfusion of blood the bleeding stops for a time, but with the reduction of these elements again the hemorrhages will recur. The blood plates have been demonstrated to be the nuclei about which thrombi form, as they produce a ferment substance which is concerned in the formation of fibrin. Such thrombi we find, of course, as hemostatic agents, instrumental in stopping hemorrhage due to bloodvessel injury.

The blood of some of the bleeding cases has a normal coagulation time, but the greater number have the coagulation time prolonged, and in some instances decomposition takes place without clotting having occurred.

When normal serum, from whatever source, is added to the blood of any of these cases which have a much prolonged coagu-

lation time, it will cause a prompt clotting. From this fact it has been reasoned that there is lacking in the blood of these individuals a kinase, or activating substance which would normally cause coagulation. If this were true we should expect to find a coagulation of the blood in the hemorrhagic areas in those cases in which the hemorrhages have been controlled by the use use of serum, but this is not the case. Clotting in the tissues does not occur after the use of normal human blood serum. The hemorrhage is stopped through some other process than that of coagulation, and the blood of existing hemorrhages is absorbed without having formed clots. The effect of normal human blood serum in controlling these hemorrhages seems to be through its nutritional effect, especially upon the endothelium lining the bloodvessels.

These hemorrhages usually occur after some special disturbance of nutrition. This disturbance may be more or less chronic, with considerable wasting away of the general tissues before the hemorrhage begins. In other cases it seems to be more acute and a condition of toxemia or septicemia. In the first instance it appears to be a species of auto-intoxication, originating in the excessive growth of pathogenic bacteria in the intestinal tract with the absorption of large quantities of toxins; in the second instance a septicemia, with a growth of bacteria in the blood stream which produces a profound synthetic poisoning. All of these conditions have the same general effect upon the nutrition of the endothelial lining of the bloodvessels. This disturbance operates to upset the balance normally maintained between the ferments and antiferments native in the cells, thereby producing conditions leading to hemorrhage. The normal human serum is a prepared food having molecules with receptors which fit the receptors of the cells of the endothelium, according to the side-chain theory of Ehrlich, which in that way is capable of being incorporated into the cell body as nourishment without any energy being wasted in the process of digestion. The nutrition being thus easily restored, the balance of ferments is reëstablished and the hemorrhages stopped.

In septic conditions normal human blood serum appears to have considerable value. I have injected four individuals having bacteremia, from the blood of whom the streptococcus was obtained by culture. Two of these individuals recovered and two died. Two cases of very grave peritonitis have also received these injections. The first, a postoperative case, on which a panhysterectomy had been done, showed marked signs of acute peritonitis on the day following the operation. Besides high fever, rapid pulse, marked abdominal tenderness and distention, she had from the second day uncontrollable vomiting. She was unable to take any nourishment whatever and was rapidly sinking. Injections of normal human blood serum in doses of 5 to 7 ounces were given daily. After the second dose was administered she showed decided improvement, in that the vomiting ceased, she was able to take liquids by mouth, the temperature receded, and the abdominal condition quickly cleared up.

The second case, a girl, aged nineteen years, curetted after abortion, ran a high temperature between 103° and 104°, with rapid pulse, shallow rapid respirations, distended tender abdomen, flushed cheeks, and dry mouth. This girl was considered to be in a hopeless condition when injections of human serum were begun. Over a period of five days the serum was administered to the amount of 300 c.c. The serum caused a decided improvement, and the patient returned slowly to her normal health.

The injections of human serum I have made in meningitis caused by the staphylococcus, streptococcus, and pneumococcus have proved of no value, possibly because these cases have been so far advanced in the degenerative processes caused in the parenchymatous organs by that bacterial toxins that recovery was impossible, though the bacteria may have been killed or their toxin neutralized.

There is a possible explanation for the beneficial action of normal human serum in septic conditions. Lack of resistance on the part of the individual to organisms may be due to one or two factors. The individual may have the ability to produce sufficient antibody, but have a deficiency in the complement

content of his serum. Again, he may have sufficient complement
but lack the ability to form antibody. In the first instance
the complement would be supplied by the normal serum injec-
tions; in the second no benefit would be derived because the
normal antibody in any given serum is a negligible quantity.
The second class should be benefited by the administration of
an appropriate antiserum, produced specifically against the infect-
ing organism. I believe we are approaching methods by which
we can fairly accurately determine which element is lacking in
the blood of septic persons, and it will not be in the very distant
future when we shall be able to direct much more intelligent
treatment in any given case.

Injections of normal human serum have proved of value in
controlling hemorrhage which occurs after operation on deeply
jaundiced persons. In coöperation with Dr. Willy Meyer, I
have made injections in such conditions with good results. Dr.
Meyer has reported this work in the *Journal of Surgery, Gyne-
cology, and Obstetrics* for August, 1911.

In passing, just a word in regard to the injections of defibrinated
blood which is advocated by some who have used it. Experiments
made by Ehrlich have demonstrated that the red blood cells
injected into the same species call forth a hemolytic body for
their digestion and removal, which he calls isolysin. In the
formation of the isolysins a certain amount of cellular energy
is consumed in their production, which is just so much extra
tax on the individual's capacity for general resistance. The
serum is so easily obtained that I can see no reason for using
whole blood, especially in babies, thereby possibly reducing the
strength of the child, already at its lowest ebb.

Transfusion, which has been so much employed, is of value,
but it is accompanied by certain dangers. Hemolysis, throm-
bosis, and embolism, all or any of which may lead to the death
of the patient, are to be feared. It is true that these are not
very frequent occurrences, but still they are common enough
to make one hesitate before using transfusion if some other
efficacious remedy can be employed. The disadvantages of

transfusion are: (1) The difficulty of the operation, which is not so simple as many suppose; (2) it is frequently necessary to use the method several times on the same subject, and in this it has certainly a great disadvantage, while, on the other hand, normal human blood serum can be repeated frequently and used indefinitely. I do not wish to disparage too much the use of transfusion, for I believe it has a field which no other agent or measure can replace. In cases of very marked depletion from prolonged hemorrhage in which the cellular elements of the blood are greatly diminished, I believe the only measure to use is transfusion, for in this operation we supply the cells necessary to the blood which are entirely lacking in any serum we may administer.

DISCUSSION.

Dr. William H. Howell: I understand that my function is to say something about the newer views upon the coagulation of blood and their possible bearing upon this topic for discussion this evening. I desire especially to take this opportunity to call your attention to the results of some work that has been going on in my laboratory during the past two or three years. In the present condition of our knowledge we may say that all theories of coagulation start from the fundamental fact that the fibrin of the clot is formed by a reaction between fibrinogen and thrombin. Our difficulty lies in understanding the origin of the thrombin. Most recent workers agree that this thrombin exists in the blood in an inactive form, which has been designated as prothrombin or thrombogen, and that before coagulation is possible this prothrombin, must be activated to thrombin. Out of the great amount of investigation upon this latter point two important facts have emerged: One is that for this activation calcium is necessary, since the blood when decalcified by oxalate solutions remains unclotted until an excess of calcium is again added. The second fact is that something is furnished by the tissues which is also concerned in and under normal conditions is necessary to this production of active thrombin. This substance furnished by the tissues has been given various names, but is designated most conveniently as thromboplastic substance or thromboplastin. In the lower vertebrates, birds, fishes, etc., we may say that the prompt coagulation of the blood is obviously dependent on this substance furnished by the tissues of the wounded surface. Blood taken from the vessels so as not

to come into contact with the tissues clots with great slowness, and if the plasma is separated promptly may not clot at all. In the mammals this action of this factor is not so evident. It can be shown that even in man's blood taken carefully directly from the vessels, clots more slowly than blood that has flowed over a wounded surface, so that in man the tissues also furnish a thromboplastin, which accelerates clotting. But in man and the other mammalia the blood itself contains a tissue, namely, the blood plates, which, on shedding of blood, rapidly disintegrate. There is every reason to believe that this tissue furnishes thromboplastin, and that the more prompt clotting of mammalian blood without the aid of the external tissues, as compared with the other vertebrates, is due to the fact that thromboplastin is furnished by this internal tissue, the blood plates, which are peculiar to mammalian blood. We may believe, therefore, that calcium and thromboplastin are both concerned in and are necessary to the formation of active thrombin. This important fact is fully considered in Morawitz's theory of coagulation, the theory which meets most approval at the present time. Morawitz assumes that the thromboplastin furnished by the tissues including the blood plates is an organic substance which functions as an activator or kinase, and he would therefore give it the specific name of thrombokinase. This organic activator, or kinase, and calcium, as an inorganic activator, coöperate in some way in activating prothrombin to thrombin. Each of these activators is necessary; one alone is insufficient. In hemophilia the tissues are lacking in thromboplastin (or thrombokinase), hence the delayed clotting. Hemophilia, therefore, is not a blood disease, but a disease affecting the protoplasm of the body in general. In the work that has been going on in my laboratory I have been convinced that this theory must be modified, and that the modification is important in controlling our attitude toward the study of the hemorrhagic diseases. In the first place I have shown conclusively that in mammalian bloods, including man, an antithrombin is a constant constituent. The data upon this and other points I have published recently in the *American Journal of Physiology*. This antithrombin is a substance which prevents the reaction between thrombin and fibrinogen, probably by combining itself with the thrombin or with the prothrombin. Its presence in blood is demonstrated by taking blood from a vein with a hypodermic syringe, oxalating it to prevent coagulation, and then centrifugalizing to obtain a clear plasma. The power of this plasma to clot is then destroyed by heating to 60° C. to precipitate its fibrinogen. If this plasma is then added in appropriate amounts to a mixture of fibrinogen and thrombin the process of clotting is thereby delayed or prevented according to the amount added. If the plasma is first heated to 85° to 90° C. its restraining

effect upon the union of fibrinogen and thrombin disappears, showing that the antithrombin belongs to the group of thermolabile substances. If now this antithrombin exists normally in the circulating blood in combination with the thrombin (or prothrombin) we can understand why the fluidity of the normal blood is protected, and the importance of the thromboplastin lies most probably not in the act of activating the pro-thrombin, as is assumed by Morawitz, but in the act of neutralizing the antithrombin and thus liberating the prothrombin. In numerous experiments the author, working with calcium-free solutions, has shown, in fact, that tissue extracts, thromboplastin, do neutralize the action of antithrombin and that, therefore, the part played by the tissues in facilitating coagulation must be explained from this point of view. The view of coagulation I would propose is that in circulating blood we have present all the necessary factors of coagulation, namely, fibrinogen, prothrombin (or thrombin), and calcium, but the reaction of coagulation cannot take place because antithrombin is also present and binds the thrombin. When blood is shed the thromboplastin furnished by the platelets and other tissues neutralizes the antithrombin and the reaction of coagulation then occurs. When excess of active thrombin is injected into the circulating blood there is a prompt formation of antithrombin (from the liver?) which prevents intravascular clotting. Experience shows that large volumes of defibrinated blood or serum, rich in active thrombin, may be introduced into the circulating blood without causing intravascular clotting. We may, therefore, believe that there is a self-regulating mechanism in the body by means of which any thrombin introduced or formed in the blood leads promptly to a formation of its antibody, antithrombin. Thrombin, in other words, acts as a hormone to stimulate the formation of antithrombin and in this way the fluidity of the blood is guaranteed under normal conditions. In the study of hemorrhagic conditions in their relations to coagulation we must take into account, therefore, four factors, namely: fibrinogen, prothrombin, calcium, and antithrombin. The variations in each of these factors, if any, should be studied in each of their conditions. I am at present engaged in a systematic investigation of the variations in the anti-thrombin contents of the blood under normal and pathological conditions and particularly in the hemorrhagic diseases. I should be very grateful for an opportunity to obtain specimens of blood from good cases of hemophilia or purpura hæmorrhagica. It seems to me that such studies are absolutely necessary as a preliminary to obtaining rational methods of treatment or to explaining the methods more in use. The excellent results reported from the use of serum injections in cases of melæna

neonatorum cannot be explained, so far as I can see, from our present knowledge of the processes of coagulation.

DR. ALBERT P. BRUBAKER: I have nothing to say that will add to the elucidation of the subject under discussion, but I would like to say a word in regard to the work of Professor Howell. I have, for special reasons, carefully followed his investigations relating to the coagulation of the blood during the last year and a half, and I am fully convinced that the existence of antithrombin has been fully established. Anyone who reads his article on "The Role of Antithrombin and Thrombino-plastin in the Coagulation of the Blood," recently published in the *American Journal of Physiology*, will, I am sure, be entirely convinced that Professor Howell is justified in stating that the fluidity of the blood in the vessels is due to the presence there of an agent, antithrombin, and that the coagulation of shed blood is due to its neutralization by the action of a substance, thrombinoplastin, furnished by the blood platelets and by the tissues.

DR. SAMUEL McC. HAMILL: I have been specially interested in the question of the etiology of these conditions, and I agree with the position taken by Dr. Nicholson that the evidence which has been collected, strongly suggests an infectious origin. In a study of these undefined illnesses of the newborn, which Dr. Nicholson and I made a few years ago, as well as in our individual studies before and since, we recovered various pathogenic organisms from the blood and tissues, which we believed were etiologically related to the clinical phenomena. Much work of a similar character has been done by competent observers.

If I understood Dr. Welch, in the earlier part of his paper he admitted a bacteriological basis for some of the cases. In his conclusions, however, he states that we are justified in considering the condition a blood disease, independent of any bacteriological relationship. My own feeling, which I have expressed elsewhere, is that the hemorrhagic manifestations under consideration may be, and in the vast majority of instances are, the result of unknown chemical changes in the blood, which are induced by the toxic action of various microörganisms. In the infant upon which Dr. Cope made a blood culture at my request, and which has been referred to by Dr. Nicholson, the infant was practically moribund at the time the culture was made. It had been ill for several days. It was universally cyanosed, respirations were labored and very irregular; the pulse was not palpable at the wrist; the extremities were cold. The removal of a little less than 2 c.c. of blood transformed this dying infant into one with normal color, regular respirations, good, full, regular radial pulse—in short, eliminated practically all symptoms except the elevated temperature, which, at the end of an hour, had fallen to normal, and

thereafter, the infant was perfectly well.   The bacteriological examination of the blood in this case gave a pure culture of streptococcus.   The explanation of this extraordinary result is just as difficult as is any attempt to explain the remarkable changes which follow the injection of blood serum.

It is probable that there are several different causative factors which must be considered in connection with the cases under discussion.   In an article by Goodall, in one of the earlier numbers of the *Archives of Pediatrics*, for the present year, he reports 3 cases having practically the same clinical picture as the cases under discussion.   In each of these the mother suffered with eclampsia, which developed almost immediately after delivery.   In 2 of them albumin had been present in the urine for some weeks.   He laid emphasis upon the time of occurrence of the eclamptic phenomena—within three days of delivery—in order to suggest the probability that at the time, the milk flow was fully established, and the infant was getting its first full feeding, the mother was eliminating toxins in large amounts.

The fact that in each of these cases the infant developed the symptom complex within a few hours of its first full feeding, seemed to justify Goodall in the belief that there had been secreted by the breasts a toxic substance which was responsible for the symptoms.   That these manifestations are not more common in eclamptic mothers, he attributes to the fact that the eclamptic phenomena ordinarily precede delivery, and that with the emptying of the uterus, there occurs a very rapid elimination of toxic products before the milk flow is established; consequently, in these cases, which represent the majority, the supposed toxins are either not eliminated through the mother's milk at all, or only in such quantity as to be ineffective.

Dr. George M. Boyd: I want first to express my appreciation, Mr. Chairman, of the papers read upon this interesting subject.   I quite agree with Dr. Nicholson as to the etiology.   I have seen some cases of malæna neonatorum, but few of late, probably due to the fact that our methods are a little better in the way of carrying out antiseptic precautions.   This bleeding should not be confused with the condition seen in syphilitic cases.   There, however, the evidences of syphilis are more or less pronounced.   In the cases I have seen the babies have been healthy, and while there has been no reason to suspect infection, they have suddenly begun to bleed.   The results of blood serum in these cases is a little short of miraculous.   I have been interested in the use of blood serum for other infectious conditions.   The use of blood serum may in the future prove to be of great help to us in the cure of infections of the puerperium and other infections of the infant.

Dr. M. Howard Fussell: I would like to know what Dr. Welch can tell us briefly of his technique of getting the serum and also the approximate mortality of these cases untreated.

Dr. Welch, closing: If I understood Dr. Nicholson to say that there is a bacteriemia as the basis of the disease I cannot agree with him. In some cases there were no bacteria in the blood at all. I have autopsied many infants born dead in which I found this hemorrhagic disease. There was present probably some disease of the placenta. I think any bacteriological condition in the colon may cause this. This is not strictly a bacteriemia but a toxemia. I think the interaction between the secretions and the meconium causes the poison which affects the endothelium.

In collecting the serum I use a U-shaped tube. The glass tubing is fitted tightly into a cork which is inserted in a filter flask. A large caliber needle, a No. 2, with a short bevel is introduced into a vein after putting a tourniquet on the arm. From twelve to fourteen ounces are collected in from four to five minutes. The wound amounts to nothing and there is no shock.

APPENDIX

ANNUAL REPORT OF THE LIBRARY COMMITTEE FOR 1911

Mr. President: In accordance with the ordinances and By-Laws of the College, I herewith submit the following report of the Library Committee for the year 1911:

Total number of volumes in the Library, including the
bound volumes and 9374 unbound "Reports" and
"Transactions" 95,896
Number of unbound "Theses" and "Dissertations" . 8,917
Number of unbound pamphlets 81,528

Included in the above total there are 2935 volumes known as "reserves," consisting of second copies of some of the more important periodical publications, and 3129 volumes more or less incomplete.

The following table shows the number of volumes in the various divisions of the Library:

	Bound.	Unbound reports and transactions.	Incomplete.	Total.
General Library .	66,202	9,374	3,082	78,658
Lewis Library . .	13,529	..	44	13,573
On permanent deposit:				
S. D. Gross Library	3,445	..	3	3,448
Library of the Obstetrical Society of Philadelphia . .	217	..	..	217
				95,896

The Library has received from all sources, during the past year, 4648 volumes, 8350 pamphlets, and 26,074 numbers of various periodicals. Of these, 1183 volumes were received in exchange.

Accessions (including 75 volumes "reserve"):

General Library 3083
Lewis Library 25
S. D. Gross Library 32

Total 3140

Duplicates for the year 1508

The "Donors" for the year ending November 1, 1911, number 430.

The following is a list of donations of twenty-five volumes or more, the gifts from the various publishing houses, and from the Philadelphia Pediatric Society:

Volumes.

Dr. A. P. C. Ashhurst 448
Dr. C. P. Noble 199
Dr. James Darrach 136
Dr. C. K. Mills 78
Dr. De F. Porter Willard 75
Dr. W. W. Farr. 72
Dr. David L. Edsall 71
Dr. Hobart A. Hare 60
Dr. J. William White 48
Miss Jane B. Evans 46
Dr. S. Weir Mitchell 35
Dr. S. McC. Hamill 35
Dr. W. M. Welch 33
Dr. F. P. Henry 25

From the publishing houses of:

P. Blakiston's Son & Co. 29
F. A. Davis Company 12
Lea & Febiger 2
J. B. Lippincott Company 39
W. B. Saunders Company 42
Salvat y Compañia (Barcelona) 2
William Wood & Co. 4

From the Philadelphia Pediatric Society 6

The Library is indebted for large gifts of pamphlets and unbound periodicals to the following:

Dr. O. H. Allis.	Dr. J. P. C. Griffith.	Dr. C. P. Noble.
Dr. A. P. C. Ashhurst.	Dr. S. McC. Hamill.	Dr. Charles O'Reilly.
Dr. M. H. Bochroch.	Dr. H. A. Hare.	Dr. David Riesman.
Dr. H. W. Cattell.	Dr. F. P. Henry.	Dr. A. C. Sautter.
Dr. Burton Chance.	Dr. A. Bern Hirsh.	Dr. G. E. de Schweinitz.
Dr. S. Solis Cohen.	Dr. E. B. Holmes.	Dr. W. G. Spiller.
Dr. Stricker Coles.	Dr. W. W. Keen.	Dr. J. J. Taylor.
Dr. J. C. Da Costa, Jr.	Dr. F. H. Klaer.	Dr. W. M. Welch.
Dr. E. P. Davis.	Dr. Morris Longstreth.	Dr. J. William White.
Dr. C. W. Dulles.	Dr. Edward Martin.	Dr. De F. Porter Willard.
Dr. D. L. Edsall.	Dr. John K. Mitchell.	Dr. C. S. Witherstine.
Dr. A. A. Eshner.	Dr. S. Weir Mitchell.	Dr. H. C. Wood.
Dr. L. F. Flick.	Dr. E. E. Montgomery.	
Dr. C. H. Frazier.	Dr. E. J. Morris.	

Also to Messrs. P. Blakiston's Son & Co., F. A. Davis Company, J. B. Lippincott Company, W. B. Saunders Company, and John Wyeth & Brother.

Of the six hundred and sixty new publications added to the Library during the past year, forty-six were written or edited by Fellows of the College.

Seventeen volumes were presented by the following authors or editors:

Dr. F. G. Benedict.	Dr. E. P. Joslin.
Dr. D. W. Cheever.	Dr. A. O. J. Kelly.
Dr. George Dock.	Dr. J. Ewing Mears.
Dr. Thomas Dwight.	Dr. William Osler.
Dr. M. H. Fischer.	Dr. H. D. Rolleston.
Dr. H. A. Hare (editor).	Dr. M. I. Wilbert.
Dr. Edward Jackson (editor).	

Twenty-nine volumes were sent by the publishers at the request of the following authors or editors:

Dr. J. M. Anders.	Dr. W. A. Newman Dorland.
Dr. H. W. Cattell.	Dr. E. B. Gleason.
Dr. E. P. Davis.	Dr. R. M. Goepp.
Dr. G. G. Davis.	Dr. J. P. C. Griffith.

Dr. W. W. Keen.	Dr. G. A. Piersol.
Dr. A. O. J. Kelly.	Dr. W. L. Pyle (editor).
Dr. Edward Martin.	Dr. C. E. de M. Sajous.
Dr. J. H. Musser.	Dr. James Thorington.
Dr. G. W. Norris.	Dr. J. C. Wilson.

Summary of the "Funds":

	Volumes purchased.	Cost.	Volumes bound.	Cost.
Henrietta Rush Fales Baker Fund	50	$186.95	9	$3.15
Luther S. Bent Fund	16	34.44	4	2.05
William T. Carter Fund . . .	48	143.97	13	7.00
Girardus Clarkson Fund . . .	7	22.06	2	1.55
Francis X. Dercum Fund . . .	54	145.14	27	25.05
John D. Griscom Fund	66	190.51	14	5.25
William F. Jenks Fund	127	461.62	27	22.25
Oliver A. Judson Fund	9	39.74		
Wm. V. and John M. Keating Fund	21	55.97	6	2.80
William W. Keen Fund . . .	63	190.44	13	8.35
Library Endowment Fund . . .	180	712.72		
Charles K. Mills Fund	1	4.15		
Weir Mitchell Fund	68	296.77		
Elizabeth K. Newcomet Fund . .	17	37.68	5	3.75
William F. Norris Fund . . .	40	153.69	20	11.50
Philadelphia Medical Society Fund	9	23.66		
Lewis Rodman Fund	36	169.82	14	9.25
John F. Weightman Fund . . .	4	17.67	3	1.25
Caspar Wistar Fund	40	173.47	7	4.60
Total	856	$3060.47	164	$107.80

Special Accounts:

	Volumes purchased.	Cost.	Volumes bound.	Cost.
Fund for completing files of journals	32	$101.38		
Fund for rare and valuable books .	14	284.49		
Journal Association	23	125.88		
New Book Fund	65	129.25		
J. Ewing Mears Account . . .	19	70.36	6	$4.35
S. D. Gross Library Account . .	30	133.81	7	10.70
Total	183	$845.17	13	$15.05

George B. Wood Fund for Library supplies, stationery, etc., $186.

There were 2198 volumes bound during the past year, an increase of 813 over the previous year. This includes all new books and current periodicals, and 753 volumes of dissertations.

Total number of visitors to the Library   6157
Fellows of the College   2955

Last year the College made a special appropriation to enable the Library Committee to have the Library kept open on legal holidays, other than Christmas, New Year's Day, Thanksgiving, and Fourth of July; and for two evenings each week, except from June 15 to September 15 inclusive. A careful record was kept of the number of visitors and of the names of the Fellows of the College. The average attendance of Fellows in the evenings, given in the annual report, was so small (about two and one-half) that it became a matter of doubt if the additional expense for this purpose was justifiable. The Library Committee determined that, as this experiment of extra opening hours had been tried for only a portion of the year, the matter should be brought before the College; and, if it was decided to continue the experiment, that the necessary appropriation be made for the purpose.

The College appropriated the sum of $694.50, in order that the Library should be kept open two evenings each week, and on legal holidays, for the same hours and time as during the year 1910, for the year 1911.

For the past twelve months, from November 1, 1910, to November 1, 1911, the Library has been kept open on five legal holidays. Total attendance, 100 [Fellows, 34]; a total average of 20, and an average for Fellows of nearly 7.

During the same period the Library has been kept open on Wednesdays and Fridays until 10 o'clock P.M. (except from June 15 to September 15). The total number of visitors after 6 o'clock P.M. was 410; of these, 185 were Fellows of the College. Total average attendance per night, nearly 5½; average for Fellows of

the College per night, $2\frac{3}{7}$. The above figures are included in the total number of visitors for the year.

Number of books consulted in the Library 16,003

The number of books reported as "consulted in the Library" includes only those supplied on application to the Librarian or his assistants. Readers have access to the bound volumes of the last ten years of the principal medical periodicals, kept on the shelves in the Reading Room; and the Fellows of the College have access to the book stacks. There are, therefore, a great many volumes consulted of which no record can be kept.

Number of books taken out 3643

All accessions of books (1114 volumes, 7486 cards) and 13 of the more important pamphlets have been catalogued, and each volume accessioned and shelf-listed; 8397 pamphlets have been examined, and 3484 retained and classified; 8383 shelf-list cards have been revised and typewritten.

The work of the "Revision of the Catalogue" has proceeded satisfactorily; 26,100 cards have been revised, typewritten, examined, and alphabeted during the year ending November 1, 1911. The revision has been completed as far as the second series of the "Index Catalogue" has been issued—"Skin-grafting"—and the work will be finished as rapidly as the remaining volumes of the alphabet appear. From inquiries made at the Surgeon-General's Office this will be, at the least, three years. The cards written at the commencement of the revision are being examined, corrected, and rewritten in accordance with the changes that have since been made in the subject headings.

The current periodical publications, including "Transactions" and "Reports," received as issued at this date, by purchase, in exchange, or as gifts from the editors and publishers, are credited and distributed as follows:

	American.	Foreign.
Henrietta Rush Fales Baker Fund . .	0	30
William T. Carter Fund	2	24
Francis X. Dercum Fund	0	3
John D. Griscom Fund	4	39
Samuel D. Gross Library Account . .	· 0	3
William F. Jenks Fund	3	36
Journal Association	1	11
Oliver A. Judson Fund	0	6
William V. and John M. Keating Fund .	0	7
William W. Keen Fund	3	23
Library Endowment Fund	5	137
J. Ewing Mears Account	0	1
Weir Mitchell Fund	1	47
Elizabeth K. Newcomet Fund . . .	0	1
William F. Norris Fund	1	4
Philadelphia Medical Society Fund . .	0	6
Lewis Rodman Fund	0	14
John F. Weightman Fund	0	4
Caspar Wistar Fund	3	17
By Purchase (General Account) . . .	8	51
In Exchange . . . . ⁄ .	87	81
Editors	109	20
Publishers	36	1
	——	——
Total	263	566

	American.	Foreign.
In addition, current numbers of periodicals are received at stated intervals, through the courtesy of the editors and editorial staff of the following journals: American Journal of the Medical Sciences, Medical Council, Therapeutic Gazette, University of Pennsylvania Medical Bulletin,	225	149
	——	——
	488	715

The total number of periodical publications, American and foreign, received at this date is 1203. The increase in subscriptions for the year 1911 is 59 (American, 11; foreign, 48).

We exchange publications with the following schools of medicine:

University of Basel.	University of Kiel.
" Berlin.	" Königsberg.
" Bern.	" Lausanne.
" Bonn.	" Leiden.
" Breslau.	" Leipzig.
" Erlangen.	" Marburg.
" Geneva.	" Rostock.
" Giessen.	" Strassburg.
" Göttigen.	" Upsala.
" Greifswald.	" Würzburg.
" Halle.	" Zurich.
" Heidelberg.	

Faculty of Medicine of Bruxelles.
" " Buenos Ayres.
" " Nancy.
" " Paris.
" " Rio de Janeiro.
" " Toulouse.

1728 Dissertations have been added to the Library during the past year.

We have received for the current year ending November 1, 1911, $286.07 in cash for the sale of duplicates; and there is a credit due us of $370.03 in cash and exchange from two New York dealers. In addition we have received books, pamphlets, and journals in exchange with the Boston Medical Library, Library of the Surgeon-General's Office, Medical Library Association, and the New York Academy of Medicine—exchanges not arranged on a cash basis. The past year has been a very successful one in the matter of exchanges—valuable books and journals have been added to our collection, in addition to the cash received, and still due us; and the money thus received it has been customary to expend in the purchase of rare books and in completing files of medical periodicals.

Amount of fines collected from November 1, 1910, to November 1, 1911, $21.85.

The following is a list of the rare medical books and works of special interest received during the past year:

Incunabula

(Total number of incunabula at this date, 160)

Articella. Comentarii. Venetiis, Locatellus, 1493. (Presented by Dr. John H. Musser.)

Bartholomæus de Pisis. Epithoma medicine. [Florentiæ, Laurentius de Morgianis, ca. 1490.] (Fund for rare books.)

Matheolus Perusinus. De memoria augenda. Romæ, Plannck [ca. 1485–90]. (Fund for rare books.)

Metlinger, B. Regiment der jungen Kinder. Augsburg, Zainer, 1473. (Fund for rare books.)

Pintor, P. De preservatione curationeque pestilentia. Rome, Silber, 1499. (Fund for rare books.)

Rhazes, A. Liber nonus. Venetiis, Papiensis, 1497. (Fund for rare books.)

Roland of Parma. De curatione pestiforum apostematum. Romæ, Udalricus Gallus [ca. 1471]. (Fund for rare books.)

Silvaticus, M. Liber pandectarum medicine. [Argentorati, Mentelin, ca. 1470.] (In exchange.)

Works of Special Interest

Alexis of Piedmont. Secrets of that Excellent Physician. London, Wight, 1595. (Fund for rare books.)

Blackmore, Sir R. Treatise upon the Smallpox. London, Clarke, 1723. (Anonymously presented.)

Chinese Punishments. Collection of Water Colors Illustrating Forms of Legal Punishment in China. (Presented by Dr. Thomas Biddle.)

Clinch, W. Historical Essay on the Rise of the Smallpox. London, Warner, 1724. (Purchased.)

Gesner, C. Nomenclator aquatilium animantium. Tiguri, Froschoverus, 1560. (Presented by Dr. A. P. C. Ashhurst.)

Harvey, William. De motu cordis et sanguinis in animalibus. Patavii, apud Sebastianum Sardum, 1643. (Presented by Dr. S. Weir Mitchell.)

Martin, B. Essay on Visual Glasses. London, 1757. (Presented by Dr. G. E. de Schweinitz.)

Russell, J. R. The History and Heroes of the Art of Medicine. 2 vols. London, Murray, 1861. (Extra illustrated.) (Presented by Dr. G. E. de Schweinitz.)

Spigelius, A. Opera quæ extant omnia. Amsterdami, Blaev, 1645. (Presented by Dr. S. Weir Mitchell.)

[Withers, P.] History of the Royal Malady. London, 1789. (Fund for rare books.)

In looking over the figures of this report and comparing them with the report for 1910, it will be seen that, while there is a decrease in the number of visitors, there has been an increase in the use of the Library (books consulted), and that the number of volumes taken out is practically the same as for the previous year.

The decrease in the number of visitors (visits to the Library) is nearly the same as in the previous report, between the years 1909 and 1910—about two thousand; and would seem to indicate that there was some foundation for the surmise made in last year's report, that the change in location had possibly affected the attendance.

The increase in the number of volumes consulted, when compared with the notable decrease in attendance, is worthy of special comment and consideration. It shows plainly a marked advance in the use of the books, with the increased advantages offered by the Library, as well as the appreciation of those who are free to consult this valuable collection.

The fact that the number of volumes taken out has remained about stationary, is readily explained by the increased use of the "Seminar rooms." Last year it was reported that the number of volumes called for and retained in these rooms for use had averaged about fifty the year round. This year, after a careful record taken, the average is shown to have increased to about one hundred and fifty volumes the year round. The Seminar room saves the carting backward and forward of books to the offices or homes of the Fellows; and, at the same time, saves a considerable amount of wear and tear on the bindings.

The record of attendance on minor legal holidays and in the evening does not show the increase expected with this full year's trial; in fact, the average number of visits by Fellows is not quite that of the previous ten months. Probably a more just comparison could be made by retaining these extra opening hours for another year, if the College sees fit to make the additional appropriation.

The large increase in the number of accessions and the number

of volumes bound, as well as the enormous decrease in the number of unbound "Theses" and "Dissertations" is accounted for by the fact that this year, with the increase of appropriation from the College over the previous year, the Library Committee have been enabled to have bound 17,292 dissertations, the accumulated exchanges of a number of years. 753 volumes, by this means, have been added to the shelves.

Last year's report showed that four volumes were missing from the shelves, and that two current journals had been abstracted from the Periodical room. The stock taking for the present year shows that the books reported missing last year have been found or replaced, and that no current periodicals have been reported missing up to the present time.

There has been no increase in the Library Endowment funds during the past year; the income received has been used for the purchase of new publications and for subscriptions. This income, about $3290, which is not half the amount required to purchase all the new medical publications and to subscribe to medical periodicals issued throughout the world, is used judiciously by the Committee; every effort is made to obtain all the important medical works issued, and also to buy all books recommended for purchase.

Respectfully submitted,

WILLIAM J. TAYLOR,
Chairman.

REPORT OF THE COMMITTEE ON THE MÜTTER MUSEUM, 1911.

The Chairman of the Mütter Committee has to report that there have been numerous contributions to the collection during the last year, among which may be especially mentioned:

1. One hundred and fifty photographs of fractures and dislocations. Presented by Dr. A. P. C. Ashhurst.

2. Family medicine case from the effects of Hon. Leonard Myers, of Philadelphia. Presented by Mr. Leonard G. Myers.

3. Surgical instruments of a native Korean surgeon. Upper half of tibia found at Port Arthur, 203 Metre Hill. Photographs, etc. Presented by Dr. Rosetta Sherwood Hall.

4. Nine brain sections showing the gross anatomy and relations of the brain. Prepared by Dr. Joseph P. Tunis. Purchased.

5. Forty microscopic sections of the brain. Prepared by C. H. Miller, of the Johns Hopkins University. Purchased.

6. A specimen of "Fracture with Unilateral Dislocation of the Twelfth Thoracic on the First Lumbar Vertebræ."

During the meetings of the Congress of Surgeons a large number of the visiting surgeons expressed their appreciation of the value of the Mütter Museum Collections.

The Mütter Lecture for 1911 was delivered in Cadwalader Hall on Friday evening, December 15, by Dr. Charles F. Nassau, Assistant Surgeon to the Jefferson Hospital, to a large and attentive audience. Subject, "Decompression in Cranial Fractures."

The Curator of the Museum, Dr. Clarence Hoffman, has been steadily at work since the last report, on the arduous undertaking of cataloging the specimens on the upper floor of the Museum so that it is ready for reference.

The Committee have been gratified by the attendance of the Fellows of the College and the visiting public.

Respectfully submitted,

GEORGE McCLELLAN,

Chairman.

LIST OF PAPERS: SECTION ON OPHTHALMOLOGY

December, 1910.

Exhibition of a Patient with a Detachment of the Retina along the Region of the Ora Serrata, by Dr. George S. Crampton.

Lymphangioma of the Conjunctiva, with Microscopic Report, by Dr. G. E. de Schweinitz, and (by invitation) Dr. Gordon J. Saxon.

A Case of Chancre of the Eyelid, and Demonstration of the Spirocheta Pallida by the Ultra Microscope, by Dr. Alexander A. Uhle and Dr. Wm. H. MacKinney; by Dr. W. T. Shoemaker.

Later History of a Previously Reported Chancre of the Conjunctiva, by Dr. G. E. de Schweinitz.

Transitory Decrease in the Static Refraction of the Eye in Diabetes, by Dr. William Zentmayer.

January, 1911.

Exhibition of a Patient with Unilateral Vertical Nystagmus, by Dr. William Zentmayer.

Exhibition of an Umbrella Perimeter (by invitation), by Dr. Wendell Reber and Dr. Joseph McCool.

Molluscum Contagiosum of the Eyelid; a supplementary report (by invitation), by Dr. Sidney L. Olsho.

Toxic Paralysis of Accommodation, by Dr. Howard F. Hansell.

Exhibition of a Patient with a Pulsating Retinal Vessel Extending Forward through the Vitreous as a Twisted Loop, by Dr. George S. Crampton.

February, 1911.

Exhibition of Two Children with Pneumococcic Infection of the Conjunctiva, by Dr. Leonard D. Frescoln.

Exhibition of a Patient with a Chorioidal Growth, by Dr. E. G. Shannon.

Exhibition of a Patient with Bilateral Chronic Glaucoma and an Intra-ocular Growth of the Right Eye, by Dr. T. B. Holloway.

Demonstration of Trachoma Bodies, by Dr. William Zentmayer and (by invitation) Dr. William T. Reese.

Exhibition of a Patient with Tuberculous Keratitis, by Dr. Frederick Krauss.

Sarcoma of the Lid, with Microscopic Studies by Dr. Gordon J. Saxon, by Dr. G. E. de Schweinitz and Dr. E. A. Shumway.

Report of a Case of Syphilitic Iritis Treated by Salvarsan, by Dr. E. A. Shumway.

March, 1911.

Exhibition of a Case of Buphthalmos, by Dr. L. D. Frescoln.

Exhibition of a Patient Showing the Results of a Bilateral Hess Operation for Congenital Ptosis, by Dr. T. B. Holloway.

Report of the Case History of a Patient with Tubercle of the Iris; Exhibition of the Patient, by Dr. Charles R. Heed.

Some Remarks on Anomalies of the Retinal Circulation, by Dr. G. E. de Schweinitz.

Exhibition of a Case of Interstitial Keratitis Successfully Treated by Salvarsan, Tuberculous Cyclitis and Chorioiditis Resulting in Cataract, Operation, by Dr. S. Lewis Ziegler.

Recurrent Iritis, Secondary Glaucoma, High Frequency Current, Iridectomy, by Dr. S. D. Risley.

April, 1911.

Exhibition of a Patient Showing the Results of Plastic Operation for Cicatricial Ectropion, following Burns of the Lids, by Dr. D. Forest Harbridge (by invitation).

Exhibition of a Baby with a Probable Ring Abscess of the Cornea, by Dr. D. Forest Harbridge (by invitation).

Exhibition of a Patient with a Dermoid Cyst of the Conjunctiva, by Dr. Charles E. G. Shannon.

Exhibition of a Patient with a Double Rupture of the Chorioid, by Dr. J. N. Risley.

Report of a Case of Syphilitic Tarsitis, by Dr. A. C. Sautter.

The Strabismus Hook, a Useful Instrument in Excision of the Lacrymal Sac, by Dr. E. A. Shumway.

Report of a Case of Orbital Tumor. (2) Exhibition of a Water-color Sketch Showing Unusual Abnormality in the Retinal Vessels, by Dr. William Campbell Posey.

Some Experiences with the Ophthalmodiaphanoscope, with Exhibition of the Lamp, by Dr. H. F. Hansell.

Some Cases Illustrating the Intra-ocular Lesions following Blows upon the Eye, by Dr. G. E. de Schweinitz.

October, 1911.

Exhibition of a Patient Showing the Late Intra-ocular Manifestations following a Contusion of the Globe, by Dr. T. B. Holloway.

Exhibition of Two Cases of Traumatic Aneurysm of the Cranial Arteries, by Dr. S. D. Risley.

Exhibition of a Patient with Unilateral Optic Atrophy and Marked Proptosis, possibly Dependent upon an Intra-orbital Growth, by Dr. William M. Sweet.

Notes Concerning the Ocular Complications in a Case of Impetigo Contagiosa, by Dr. H. F. Hansell.

Exhibition of a Case of Marginal Degeneration of the Cornea, by Dr. William Zentmayer.

November, 1911.

COMBINED MEETING OF THE SECTIONS ON OPHTHALMOLOGY
AND OTOLOGY AND LARYNGOLOGY.

Meeting held during the Second Annual Congress of the Clinical Surgeons of North America.

By invitation the following papers were presented:

The Surgery of the Sinuses and its Relation to Orbital Complication, by Dr. Joseph H. Bryan, Washington, D. C.

The Relation between Otitic and Intracranial Diseases, by Dr. Gorham Bacon, New York.

The Newer Operations for Glaucoma, by Dr. John E. Weeks, New York.

THOMAS B. HOLLOWAY,
Clerk.

LIST OF PAPERS: SECTION ON OTOLOGY AND LARYNGOLOGY

December 21, 1910.

Dr. George B. Wood: (1) Report of a Case of Circumscribed Labyrinthitis. Presentation of patient. (2) Description of an Operation for Correcting Anterior Deflection of the Septal Cartilage. Demonstration of patient.

Dr. George Fetterolf: A Case of Advanced Laryngeal Tuberculosis Treated by Galvanopuncture. Exhibition of patient.

Dr. B. Alexander Randall: A Fatal Case of Gradenigo Syndrome with Ill-declared Sinus Thrombosis and Cerebellar Abscess.

January 18, 1911.

Dr. James Babbit: Report of a Secondary Hemorrhage Occurring Ten Days after Tonsillectomy. Presentation of patient.

Dr. Ralph Butler: Presentation of Three Patients Operated upon for Deformity of the External Nose.

Dr. A. W. Watson: Report of a Case of Status Lymphaticus, with Autopsy.

February 15, 1911.

Dr. Benjamin Parish: Report of a Case of Recurrent Papilloma of the Larynx. Exhibition of the case.

Dr. B. Alexander Randall: The More Efficient Measures of Aural Massage.

Dr. George C. Stout: A New Method of Diagnosticating and Treating Sinus Inflammations.

March 15, 1911.

Dr. Francis R. Packard: Presentation of a Case of Carcinoma of the Larynx after Operation.

Dr. Ralph Butler: Presentation of a Case of Thrombosis of the Left Vertebral Artery Showing Paralysis of the Palate, Pharynx, and Larynx.

Dr. Joseph Gibb: Report of a Case of Primary Carcinoma of the Maxillary Antrum.

April 19, 1911.

Dr. S. MacCuen Smith: Presentation of an Interesting Case of Sinus Thrombosis.

Dr. George B. Wood: Report of a Case of Acute Frontal Sinusitis with Perforation of the External Plate in Three Days. Presentation of patient.

Dr. Isaac Jones (by invitation): Report of Two Cases of Sarcoma of the Nasopharynx. Presentation of patients.

May 17, 1911.

Dr. Charles P. Grayson: Some Clinical Notes of Five Cases of Laryngeal Papilloma in the Adult.

Dr. E. L. Vansant: Report of a Case of Paralysis of the Left Vocal Cord Due to Pulmonary Lesions, with Report on Some Other Cases.

Dr. George Fetterolf: The Thoracic Course and Relations of the Left Recurrent Laryngeal Nerve, with Reference to Paralysis of the Vocal Cord. Illustrated by frozen sections and lantern slides.

October 18, 1911.

Dr. Walter Roberts: Report of a Case of Recurrent Papilloma of the Larynx and Trachea. Presentation of patient.

Dr. George Fetterolf: Report of Two Cases of Salivary Calculus, with Exhibition of Specimens.

Dr. G. Hudson-Makuen: Word Deafness in its Relation to Defects of Speech, with Exhibition of a Patient.

November 15, 1911.

COMBINED MEETING OF THE SECTIONS ON OPHTHALMOLOGY
AND OTOLOGY AND LARYNGOLOGY.

Dr. Joseph Bryan, Washington, D. C.: A Further Contribution to the Study of Diseases of the Accessory Sinuses in Relation to Diseases of the Eye and the Surgical Measures to be Adopted for their Relief.

Dr. Gorham Bacon, New York: The Relation between Otitic and Intracranial Diseases.

Dr. John E. Weeks, New York: The Newer Operations for Glaucoma.

RALPH BUTLER,
Clerk.

LIST OF PAPERS: SECTION ON GENERAL MEDICINE

January, 1911.

Two papers on the Electrocardiogram in Relation to the Physiology, Pathology, and Diagnosis of Heart Disease, by Dr. Lewellys F. Barker, of the Johns Hopkins University (by invitation) and by Dr. Walter B. James, of the College of Physicians and Surgeons, Columbia University (by invitation).

February, 1911.

Malignant Disease of the Lung (specimen), by Dr. H. R. M. Landis.

Pneumothorax with Acute Abdominal Symptoms, by Dr. E. J. G. Beardsley.

Three Unusual Cases of Pulmonary Disease with Autopsies, by Dr. R. T. Devereux (by invitation).

Indications for Surgical Intervention in Pulmonary Disease, by Dr. Samuel Robinson, of Boston (by invitation).

March, 1911.

A Specimen of Aneurysm Treated by Wiring, by Dr. James Tyson.

A Case of Heart Block with Exhibition of Pulse Tracings, by Dr. Wm. Pepper.

A Patient with Heart Block with Tracings from the Same, by Dr. George W. Norris and Dr. George T. Lukens (by invitation).

Pulse Tracings from a Case of Auricular Fibrillation Coming on during an Attack of Croupous Pneumonia and Disappearing with the Crisis, by Dr. George W. Norris.

Gastric and Duodenal Adhesions in the Gall-bladder Region and Their Causes (lantern demonstration), by Dr. George E. Pfahler.

April, 1911.

Two Cases of Dupuytren's Disease with Remarks on its Pathogenesis, by Dr. Alfred Gordon.

Studies of Blood Pressure in Pneumonia, with Especial Reference to the Relation of Blood Pressure to the Pulse Rate, by Dr. E. H. Goodman and Dr. R. Pitman (by invitation).

Report of a Case Illustrating the Difficulties of Diagnosticating the Pulmonary Conditions in the Presence of Heart Disease, by Dr. Charles M. Montgomery.

On the Insidious Onset of Pneumothorax, by Dr. O. H. Perry Pepper (by invitation).

A Clinical Study of 44 Cases of Pneumothorax Occurring in the Course of Pulmonary Tuberculosis, by Dr. John M. Cruice.

May, 1911.

A Case of Acromegaly, by Dr. David Riesman.

Chlorosis (Report of Cases), by Dr. H. K. Hill.

Two Cases of Catarrhal Laryngitis Requiring Intubation, by Dr. J. F. Ullom.

An Epidemic of Laboratory Diphtheria at the Presbyterian Hospital, by Dr. DeWitt (by invitation).

A Case of Typhoid Sepsis and a Case of Typhoid Fever Treated by Vaccine, by Dr. Joseph Sailer.

Studies on the Excretion of Salicylic Acid and Hexamethylenamine in the Sputum, by Dr. E. H. Goodman and Mr. J. I. Armstrong (by invitation).

Is There a Mitral Stenosis of Traumatic Origin? by Dr. David Riesman.

A Case of Cirrhosis of the Liver with a Venus Hum in the Epigastrium which Disappears on Pressure with the Stethoscope, by Dr. J. N. Henry.

October, 1911.

The Effect of Caffeine on the Circulatory and Muscular Systems, by Dr. H. C. Wood, Jr.

The Effect of Caffeine on Nitrogenous Excretion and Partition, by Dr. C. B. Farr and W. H. Welker, PhD. (by invitation).

The Influence of Caffeine on Mental and Motor Efficiency, by H. I. Hollingsworth, PhD., of Barnard College (by invitation).

November, 1911.

Native Chinese Medicine (illustrated by specimens and lantern slides), by Dr. William W. Cadbury (by invitation). •

The Value of Sections and Dissections of the Hardened Body in the

Teaching of Physical Diagnosis (illustrated by lantern slides), by Dr. George Fetterolf and Dr. H. R. M. Landis.

Vaccination against Typhoid Fever in the United States Army, by Captain A. W. Williams, U. S. A. Medical Corps (by invitation).

A Case of Persistent Hemoptysis with Well-marked Presystolic Thrill and Murmur following Violent Contusion of the Chest, by Dr. J. C. Wilson.

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C. B. FARR,
Clerk.

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